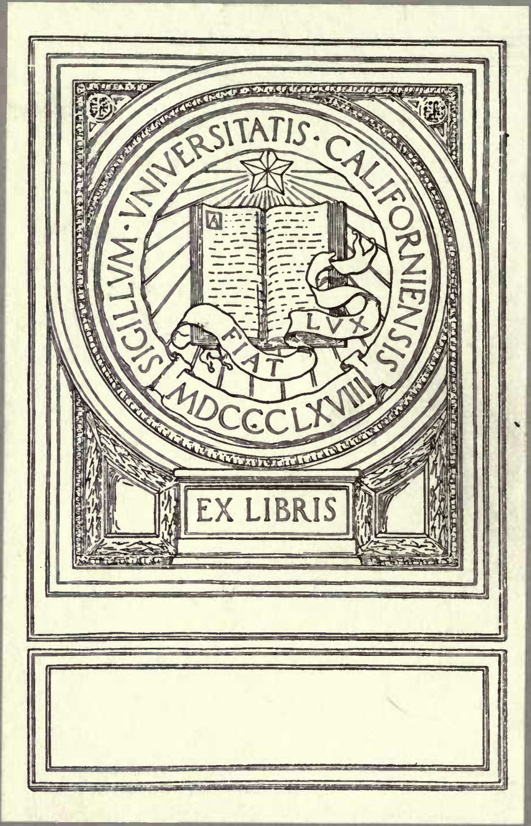
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PASTEUR AND HIS WORK

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Pasteur in his Laboratory
(after Edelfelt)

De toutes les maladies virulentes la rage
est la plus facile a prévenir.
L. Pasteur

PASTEUR AND HIS WORK

By L. DESCOUR

(*Médicin Inspecteur de l'Armée*)

TRANSLATED FROM THE FRENCH BY

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PREFACE TO THE SECOND EDITION

Dr. Émile Roux, Member of the Academy of Science and of the Academy of Medicine, Director of the Pasteur Institute, who was one of Pasteur's dearest disciples and his daily collaborator through all that period of his life which was most fertile in discoveries, has presented this book to both Academies.

The following lines are taken from his speech to the Academy of Medicine during the sitting of June 21, 1921 :—

" M. Descour has been good enough to submit the proofs of his book to me ; I have read them with the greatest interest, so attractive is Pasteur's work even to those already familiar with it, and also because M. Descour has described it with a precision, an orderliness, and an emotion worthy of so great a subject. In a volume of less than three hundred pages, the author has been able to relate what nobody should be ignorant of in Pasteur's life, and what all who are engaged in scientific work should know of the achievements of this great man."

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Some men have received at birth such magnificent and exceptional gifts that they form only discouraging examples to the rest of mankind. Who would dare to take a Pascal or a Newton as model?

Pasteur is more approachable. He was to begin with much like the rest of us. His genius, the fruit of clear reasoning and persevering work, enlightens without dazzling us. This makes his history more interesting.

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PASTEUR AND HIS WORK

CHAPTER I

EARLY YEARS

Louis Pasteur was born at Dôle, in a little house in the Rue des Tanneurs, December 17, 1822. He had three sisters. His father, a non-commissioned officer of the Empire, who had been created Chevalier of the Legion of Honour on the battlefield, had, on leaving the army, resumed the trade of tanner, which had been that of his family for two generations. His mother was the daughter of simple market-gardeners.

He was still quite a child when his parents came to live in Arbois. At the École Primaire, and later at the College of Arbois, Louis Pasteur was a merely average pupil. He showed a rather marked taste for drawing. A few successful efforts in chalks and in charcoal seemed to foretell an artistic career. However, the Principal of the college, having an intuition of the worth of this attentive, thoughtful, and conscientious child, who had so much will-power, and was so capable of enthusiasm, advised him to work with a view to entering an École Normale Supérieure.

His father and mother, particularly his father, had a great influence over the formation of his character. "The old non-commissioned officer," writes M. Duclaux in his *Louis Pasteur* (*Annales de l'Institut Pasteur*, 1895), "had become a tanner, a small tanner, inexpert in matters which did not interest him, a rough worker at a rough trade, a stubborn, obstinate man. This soldier of 1815 preserved all through his life the faith and ardent generosity of a volunteer of the Republic. The idea of *la patrie*, his beloved country, vanquished and humiliated, the necessity for its rehabilitation ; the efforts to be made to set it once more upon its feet, and the devotion which all were bound to bring to the performance of this great work ; these were the first impressions received by the infant brain of Pasteur. His father constantly recurred to them, under many different forms, with the same persistence with which he pursued his daily toil, and as his whole life was in conformity with his talk, his influence had the penetrating power of spring rain. His son's life remained impregnated with it, and that is the reason why Pasteur never felt in his first efforts, in his growing reputation and in his final celebrity, anything but a more and more complete gratification of his patriotism."

In 1839 Louis Pasteur left the College of Arbois, where the classes did not go beyond *rhetoric*, for that of Besançon. There he found, by way of professor, a worthy old man, who peacefully taught chemistry by following the text of his book line by line. His classes were little more than recitation lessons. Pasteur, however, being of a more inquiring mind than his fellows, needed to understand and see clearly. He often asked embarrassing questions, so that at last the professor requested him to hold his tongue, saying that he was reversing rôles, and that it was not the pupil's place to put his master through a sort of examination. Pasteur tried to satisfy his craving for learning by asking for a few lessons from a chemist in the town who had gained the reputation of a man of science, because a memorandum signed by him had been honoured with a place in the *Annales de Chemie et de Physique.*

At the end of the scholastic year Louis Pasteur successfully passed his *baccalauréat ès lettres.* In 1842 he became *bachelier ès sciences* with the least possible distinction, the future chemist receiving for his chemical paper the comment *médiocre.* A few weeks later he was placed fifteenth out of twenty-two candidates admitted to the École Normale Supérieure. Dissatisfied with this rank, he resigned his place and decided to compete again in the following year.

The example of a schoolfellow who took first place at the École Normale after a course of study at a Paris *Lycée*, made him abandon the Royal College of Besançon. He managed to get admitted as pupil and teacher—the services of one paying the greater part of the fees of the other—at an institution conducted by a compatriot from the Franche-Comté in the Impasse des Feuillantines.

With two other students he occupied a stone-paved room, which was very cold in winter, and he notes, with characteristic exactitude, that he and his comrades have hired a stove for eight francs, have twice bought wood, and that he has allowed himself the luxury of a cloth, costing two francs, for his table, as the holes and cracks in it prevented him from writing.[1]

Pasteur followed the course of studies at the Lycée Saint Louis and found time to go to the Sorbonne to hear the lectures of Jean-Baptiste Dumas, the great chemist, whose learning and eloquence carried him away. At the end of the year he took fourth place at the École Normale, where he proved a satisfactory pupil and a furious worker, but did not distinguish himself by any exceptional merit. He was placed seventh in the *examen de licence*, third in the *concours d'agrégation* out of the four candidates passed, and when he presented himself for the degree of Doctor, August 23, 1847, he only obtained for his two treatises one white ball and two red.

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[1] These details are borrowed from the *Life of Pasteur*, by René Vallery-Radot, a work of the greatest documentary value, a monument raised in Pasteur's honour by the man he chose to be his daughter's husband and who became like a real son to him.

CHAPTER II

STUDIES ON CRYSTALLOGRAPHY[1]—FIRST DISCOVERY

PASTEUR had entitled his treatise in physics *Study of the phenomena related to the rotatory polarization of liquids.*

This question had interested him for a long time. He had read in 1844, in the *Reports of the Academy of Science,* a note that Mitscherlich, a learned chemist of Berlin, had just published on the subject of the tartrate and paratartrate of sodium and ammonia. These two double salts "have the same chemical composition, the same crystalline form, with the same angles, the same specific gravity, the same double refraction, and in consequence the same angle between the optical axes. Dissolved in water, their refraction is the same, but the dissolved tartrate turns the plane of polarized light, and the paratartrate is inactive."

Why between two substances almost identical is there this single difference, and to what in the *intimate* structure of each can it be related ? Mitscherlich had not even attempted to answer this question, neither had Biot, a Member of the Institute, and Professor of the College of France, who had made such numerous and wonderful researches on the polarization of light.

Pasteur recalled with admiration the work of Malus, a young Captain of French Engineers, to whom we owe the knowledge of these phenomena, the origin of a new science. Pasteur sometimes passed under the windows of the little room in the Rue d'Enfer, where Malus, in 1808, made his first observations. At that time everybody thought that light reflected from a polished surface changed its direction without changing its properties.

---

[1] Chapters I and II are difficult reading. They are not essential in order to gain a knowledge of the most useful and interesting part of Pasteur's work, that which constitutes his incomparable greatness. Nevertheless Pasteur attached great importance to these first studies ; he had for them a special affection, and often expressed regret that he was unable to continue them.

Huyghens had observed, two centuries previously, that a ray emanating directly from a luminous source acquires new qualities in traversing Iceland-spar. This crystal doubles the image of objects, because it gives two refracted rays for each incident one; if one observes through a spar the flame of a candle (which emits what is known as direct light) one always sees two flames of equal brightness. If through a second spar one observes one or other of these two flames (which are composed of refracted light), either one may see a single image only, or one may see two, but in the latter case the two images are not of the same intensity, and moreover their intensity varies with the position given to the crystal. In this way the light emerging from Iceland-spar differs from what it was before entering. This modification had been attributed to a particular property of the spar, and the discovery, which appeared unimportant, had remained without practical application when Malus resumed the study of double refraction. He first saw that all doubly refracting crystals can, like Iceland-spar, give a character to the refracted ray which distinguishes it from the direct ray. One day he observed from his window, through a tourmaline, the rays of the setting sun reflected on the panes of the Luxembourg palace. He observed that on rotating the tourmaline on a plane perpendicular to the rays, he could diminish the light to extinction, that is to say, the rays in a certain position no longer pass through the crystal. No such result is produced with direct light. Reflected light therefore had acquired new properties, as does light when refracted.

Newton explained luminous phenomena by supposing that the sun and other luminous bodies emit in a straight line and in all directions material particles, exceedingly minute and endowed with great velocity. These particles striking the eye, directly or indirectly, give us a sensation of light. When he learnt the facts observed by Huyghens, Newton saw that his hypothesis was too simple, by itself, to account for the qualities acquired by a refracted ray. He completed it by the supposition that the luminous particles have poles opposed to one another, and possessing different properties. Under ordinary conditions, these innumerable poles are oriented in every possible fashion, with the result that being symmetrical, the ray presents in all directions the *same* properties; but it is conceivable that the orientation of the poles in certain particular ways can give to the ray in corresponding directions *new* properties.

Malus adopted Newton's idea, and explained the phenomenon which he had discovered by the supposition that the reflection of a ray has the effect of orienting the poles of luminous particles in the same direction; in order clearly to distinguish this character, he called the ray so modified a *polarized* ray. The following comparison illustrates quite roughly the conception of Malus.

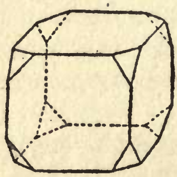
Suppose one throws some wheat-grains into a sieve, the meshes of which, of the same shape as the grain, are large enough to allow it to pass through, when it presents its long axis in the direction of those of the meshes, but, on the other hand, retain it when it presents its long axis transversely. If one throw grains oriented in every sort of direction, some will pass through and others be retained. One can imagine, however, that if these grains were of magnetic steel they would all take the direction north and south, as does the compass-needle; if one gave this direction to the interstices of the sieve, all would pass through, but if one gave the direction east and west to the interstices, all would be retained. The network of crystalline molecules acts as a sieve, and in accordance with the position given to the crystal, allows or refuses passage to the polarized luminous particles. From this it follows that the manner in which a polarized ray traverses a crystalline plate corresponds to the *intimate* structure of the crystal. The plane of reflection determined by the incident and polarized ray has been called the plane of polarization.

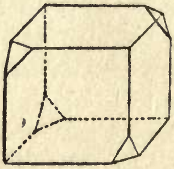
Supposing that a pendulum oscillates before a wall in a direction perpendicular to the plane of the wall. Allow the oscillating rod to be modified, not in its form, but in its *intimate* constitution—we may call it for convenience *polarized*, then the plane of oscillation, *employing the same convention*, becomes the *plane of polarization*—modified in such a way that, looked at through a layer of crystal, it appears to move in a plane making with the original plane an angle open to our right, we should say that the plane of oscillation, or of polarization, is deviated to the right.

Malus made remarkable studies in the polarization of light; he died at the age of thirty-seven. Binot and Arago especially distinguished themselves among those who continued his researches. They observed, by means of appropriate apparatus, that certain crystals and certain solutions turn the plane of polarization to the right, whereas other crystals and other solutions turn the plane of polarization to the left, and this new phenomenon, this *rotatory power*, becomes in many substances a valuable characteristic for identification. Biot had observed, in particular, that for a given solution the deviation does not depend on the direction in which the polarized ray traverses the solution, neither does it depend on the manner in which the molecules of dissolved salt are disposed in the solvent, since the agitation of the fluid has no influence on the direction or degree of the deviation. The action exercised on the polarized ray can thus only be attributed to the form of the molecule itself and its innate constitution. All substances whose solutions were then known to deviate light belonged to the animal or vegetable kingdom: such as sugar, tartaric acid, and albumen; and this led to the idea that rotatory power was intimately connected with the phenomena of animal and vegetable life.

Pasteur, who was passionately interested in these investigations, was haunted by the problem which Mitscherlich's note had raised: why have not tartrates and paratartrates which present crystals of the same form and composition the same action on polarized light? This note upset all his ideas, as a conscientious student, of logic and accuracy. "I could not understand," he said later, "that two substances could be as much alike as Mitscherlich said without being identical. To be astonished at anything is the first movement of the mind towards discovery." With the object of neglecting no side of the question, the importance of which he realized, he set himself to study the crystalline forms of tartaric acid and the tartrates. Delafosse, the learned professor of the Faculty of Science, had given him a taste for crystallography, a science wholly French, created by his master, the Abbé René Haüy, brother of the famous educator of the blind.

Haüy had established and formulated the law that when a crystalline form is modified, when it undergoes a *truncation*, this truncation is repeated in the same manner on all its external parts which appear to be identical, and which for that reason he believed to *be* identical, with one another. For example, in crystals of the cubical system one finds the *cube épointé*, whose eight angles are replaced by little *facets* inclined at the same angle to the adjacent surfaces. Haüy, however, had clearly seen that the law which speaks of *symmetry* allows of exceptions; he had discovered cubical crystals, four of whose angles only, placed alternately above and below the lateral edges, were without points; under these conditions one never finds two facets at the extremities of the same edge of the cube. This modification, applying only to half of the similar elements, was called *hemihedral*. Haüy remarked it particularly in the prismatic crystals of quartz, and noted in this connection an


Cube *épointé*.


Hemihedral Cube.

interesting fact. He oriented prisms in the same manner, in accordance with a well-defined convention, and established the fact that each crystal had all its hemihedral facets inclined in the same relation to the edge which carried them; but, in regard to some of the facets, they were placed to the right of the observer, and others to the left. Haüy called *plagihedra* all those crystals with hemihedral facets, and distinguished them as dextro and lævo plagihedra.

In another direction, Biot, studying the same prisms from the point of view of their action on polarized light, noted that some deviated the plane of polarization to the right and others to the left; this he expressed by calling the one right-handed and the other left-handed quartzes, but he did not think of correlating his polarimetric observations with those, purely crystallographic, made by Haüy. It was an English physicist, John Herschell, who called attention some years later to the interest of this relationship, and so discovered the connection existing between crystalline form and rotatory power.

Delafosse had the credit of being the first to give an explanation of hemihedry by showing that to establish the identity of certain sides of a crystal, it is not enough to consider their geometric form, it is also necessary that the sides be identical in their physical relationship, that is to say, that they have the same structure and the same molecular constitution; in other words, crystals are not geometrical entities, their form is only the expression of the properties of their substance, and hemihedry, which is a regulated derogation of the law of symmetry, seems to indicate that certain elements, though similar geometrically, differ in their fundamental structure.

Among crystals viewed from all their faces or facets, the greater number have one or many planes of symmetry; these same crystals, modified by hemihedry, have none. This is a fact observable in many common objects, and it allows of useful distinctions. A chair has one plane of symmetry, that perpendicular to the back, and dividing it in half. On each side of and equi-distant from this plane are identical elements. It is usual to say, somewhat inaccurately, that this chair, placed before a looking-glass, gives an image superimposable on itself. The superimposition of two solids, point to point, is only conceivable in geometry, where the possibility is assumed of two solids penetrating one another, and occupying simultaneously the same portion of space; one can only say that the same cover would be exactly adapted to a chair and its reflection.

That which characterizes an object possessing a plane of symmetry is that the object and its reflection in a mirror could be enclosed in the same mould. Our hands have no plane of symmetry, no plane dividing one hand can divide it into two similar halves; in a mirror the image of a right hand is a left, and the right-hand glove could not cover the image of this hand.

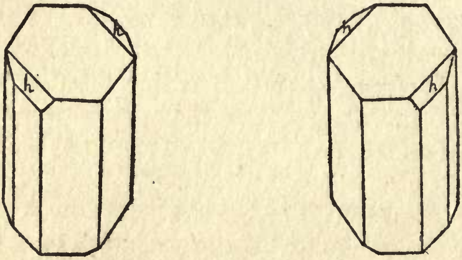
Pasteur attached great importance to these considerations of symmetry, as well as to the relation established since John Herschell between hemihedry and rotatory power. He was working in accordance with these ideas when, while examining tartaric acid and the tartrates with that careful exactitude which he brought to all his investigations, he perceived that these crystals presented on half of their corresponding edges facets which are often so small that it is difficult to perceive them, so that they had not been noticed by Mitscherlich or any other crystallographer. This was a ray of light.

Pasteur asked himself whether this hitherto unobserved hemihedry might not contain the solution of the problem. He examined numerous tartaric crystals—all were hemihedral; they were, in accordance with the definition of Haüy, dextro-plagihedra; it is therefore natural that they should deviate the plane of polarization to the right. The crystals of paratartrates presented facets analogous to those of the tartrates, but arranged according to the law of symmetry, it was no longer half but all the similar edges which bore a truncation. It was therefore not surprising that these paratartrates of regular form did not possess the rotatory power of the hemihedral tartrates.

"All of a sudden," relates Pasteur, "I was filled with emotion. The great surprise which Mitscherlich's note on the tartrates and paratartrates had occasioned me, had always remained. In spite of his very careful study, I said to myself, of these two compounds, Mitscherlich cannot have perceived that the tartrate is dyssymmetrical, as it should be ; nor can he have seen that the paratartrate is not, which is equally probable. At once, with feverish activity, I prepared the double tartrate of sodium and ammonia, and the corresponding paratartrate, and set about comparing their crystalline forms ; with the preconceived idea which I had just formed, of dyssymmetry in the tartrate, and the absence of dyssymmetry in the paratartrate form. Thus, thought I, all will be explained ; Mitscherlich's note will be no longer mysterious ; dyssymmetry in the form of the tartrate will correspond to its optical dyssymmetry ; the absence of dyssymmetry in the paratartrate will correspond to the absence of activity of this salt on polarized light, to its optical indifference. I discovered, in fact, that the tartrate of ammonia did bear facets betraying dyssymmetry ; but when I came to the crystalline form of the paratartrates I had a momentary shock, for all these crystals bore dyssymmetrical facets."

Was this paratartrate going to invalidate the law of the relation between rotatory power and hemihedry ? Pasteur had too strong a conviction to rest content with this idea. He examined more closely the hemihedral crystals, the complex shape of which concealed a mystery. He selected the largest of them, and, comparing them two by two—after having taken care to orient them in relation to a vertical plane which divided them into two halves, right and left—he perceived that the hemihedral facets were not arranged in the same manner. In some of them the anterior dyssymetrical facets, that nearest to himself, was inclined to the right in relation to the plane of orientation ; in others, this facet was inclined to the left. " In other words, the paratartrate showed that it was made up of two sorts of crystals, one dyssymmetrical to its right, the other to the left." Pasteur immediately supposed that these dyssymmetries of form must correspond with dyssymmetry of molecular constitution. From that moment he lived in that fever of the investigator who feels himself on the track of a discovery.

He took the hemihedral crystals and separated those whose homologous facets were inversely placed, distinguishing between those with facets right and left. The first resembled the tartaric crystal in all points; would they not possess the same power of deviating the plane of polarization to the right? And would not the others deviate the plane to the left? And would not the mixture in equal parts of the dextro and lævo crystals give a neutral solution in which the opposed actions would counteract each other? A prey to the liveliest emotion, Pasteur performed these different experiments. All his previsions were confirmed. What joy! He left the laboratory, and meeting a comrade outside, in the ardour of his enthusiasm he embraced him . . . it was his first victory!



Paratartrate of soda and ammonia
formed by an equal mixture of hemihedral crystals
Lævo-Tartrate Dextro-Tartrate
The anterior hemihedral facet *h* is on the left of the observer in the lævo-tartrate, and on his right in the dextro-tartrate.

In spite of Pasteur's modesty, his masters had not been long in recognizing the worth of a pupil who was so possessed by the desire to learn, and whose brilliant and accurate intellect did not allow itself to be repelled by difficulties, but on the contrary sought for them in order to conquer them; who was not afraid of bold hypotheses, but knew how to guard against rash conclusions. He himself said, when facing conjectures of the utmost probability: "It is possible, but one must see, one must dwell long on a subject." This prudence had served him well.

Balard, an old pharmacy pupil, Professor of Chemistry at Montpellier (where he had made himself famous in his chemical laboratory, at the age of twenty-four, by the discovery of bromine), Director of Lectures at the École Normale, then member of the Institute, and Professor at the Sorbonne, highly appreciated Pasteur; he had him attached as *agrégé* to his laboratory, and knew how to keep him there when the Minister wished to send him as Professor of Physics to the College of Tournon. With southern enthusiasm, which some thought exaggerated, he related his pupil's achievements to Jean Baptiste Dumas, and to the venerable Biot, who was then seventy-four years old. Biot was sceptical. How could a young man, who had scarcely left school, be able to solve a problem which had defeated Mitscherlich, and of whose solution he, Biot, had not even caught a glimpse?

Pasteur wrote to Biot, whom he did not yet know, respectfully requesting him to be good enough to verify his results. Biot bade him come to the Collège de France, where he lived. He submitted to him a paratartaric acid, the perfect indifference of which he had carefully verified, and invited him to prepare, under his eye, with the sodium and ammonium given him, the double salt which was to serve for the experiment. The liquor obtained was shut up in one of the cupboards in the room, and left to evaporate slowly. These minute precautions did doubtless not imply that Biot distrusted Balard's pupil, they were due to the natural prudence of the man of science wishing to guard against any possibility of deception.

Some days later Pasteur returned; chose from the saline solution the finest crystals, and demonstrated to Biot the hemihedral facets arranged inversely, which allowed of separation into two groups, right and left. Biot solemnly questioned Pasteur: "You definitely affirm that the crystals placed on my right will deviate the plane of polarization to the right, and the others to the left ? "

"I do affirm it."

Biot prepared the solutions, putting into the polariscope the solution which should deviate to the left, and made an observation. The deviation predicted clearly showed itself.

The old man, deeply moved, took Pasteur's arm, and said in his solemn voice :

"My dear boy, I have so loved science all my life that this makes my heart beat."

"It was in fact evident," said Pasteur when describing this memorable séance, "that the brightest light had just been thrown on the subject of rotatory polarization and hemihedry in crystals ; that a new class of isomeric substances had been discovered ; that the constitution of paratartaric acid, unexpected and previously unparalleled, was made clear ; that, in a word, a great road, new and unforeseen, was opened to science."[1]

In the first five months of the year 1848 Pasteur had addressed to the Academy of Science four important communications on the subject of crystallography ; nevertheless the representations of Biot and Balard could not prevent his being nominated Professor of Physics at the College of Dijon, and torn from his beloved work in the laboratory.

In his new sphere he showed himself as the conscientious man he had always been, devoting most of his time to preparing his lessons and in making them clear and attractive. He was satisfied when, in a class of eighty pupils, he had succeeded, by increasing the number of his experiments, in keeping awake the attention of all. But it was not in this direction that his path lay, and fortunately his former masters succeeded in getting him appointed to a post where he could resume his interrupted studies.

[1] Quoted by René Vallery-Radot, *op. cit.*, p. 47.

CHAPTER III

PASTEUR'S MARRIAGE

In the month of January 1849 Pasteur was appointed to the Chair of Chemistry of the Faculty of Strasbourg.

One of his first visits was to the Rector of the Academy, M. Laurent. Pasteur had written to his father that he did not think of marrying for a long time. The sight of one of the Rector's daughters soon made him forget this resolution. A fortnight after his arrival he wrote to M. Laurent to announce an imminent proposal of marriage and to give him some personal information :

"My father is a tanner at Arbois, a little town in the Jura. My sisters help my father in his business and in the house, taking the place of the mother whom we had the misfortune to lose last May. My family is comfortably off, but not rich. I estimate the value of all that we possess at not more than fifty thousand francs, and as regards myself I have long ago resolved to surrender to my sisters the whole share which would eventually be mine. I have therefore no fortune. All that I possess is good health, a good heart, and my position in the University. I left the École Normale two years ago with a degree in Science. Six months later I took my Doctor's degree, and have since presented to the Academy several works which have been very well received, especially the last. A very favourable report, which I have the honour to submit to you with this letter, has been made on this work. That, Sir, is my present position. As for the future I can only say that unless my tastes should undergo a complete change I shall devote myself to chemical research. My ambition is to return to Paris as soon as I have achieved some reputation by my scientific labours. M. Biot has several times advised me to think seriously of the Institute. In ten or fifteen years I might aspire to that if I continue working assiduously. This is a mere dream, however, and it is not that which makes me love science as science."[1]

Mlle Marie Laurent refused to give an immediate answer, and Pasteur wrote anxiously to Mme Laurent:

"I am afraid that Mlle Marie attaches too much importance to first impressions, which can only be unfavourable to me. There is nothing in me to attract a young girl, but memory tells me that when people have known me well, they have liked me." And to her whom in his heart he already called his fiancée he says:

"All that I ask you, Mademoiselle, is not to judge me too quickly. You might be mistaken. Time will show you that under this cold and shy exterior there is a heart full of affection for you."

The proposal was accepted, and the marriage took place on May 29, 1849.

There is a legend of its having been necessary to run to Pasteur's laboratory to warn him that the hour fixed for the ceremony was approaching. It is perhaps only a legend, but Pasteur had other moments of forgetfulness. Chappuis, one of his best and most intimate friends, admitted that Mme Pasteur deserved some credit for accepting a husband: "such as he was, with this habit of living in his laboratory, with his passion for work, and his tendency to be absorbed in thought, and for having never turned him from his course, or been too jealous of Science."

Great entertainments took place at Strasbourg on the occasion of a visit from the Prince President. The inhabitants of the neighbourhood marched in procession, headed by banners. On the day of the Prince's arrival Chappuis relates: "Pasteur returns to his laboratory for a few minutes, as he states, and then he forgets the passing hours, and Mme Pasteur, who had waited for him in vain, and missed the pleasure of attending the festivities, says not a word of reproach when her husband, in the evening, simply remarks : What would you have ? I could not interrupt my experiments."

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[1] Quoted by René Vallery-Radot, *op. cit.*, pp. 55, 56, 57.

Pasteur's father admired the young wife who could pardon such absentmindedness with such kindly indulgence. She only opposed, and that with the greatest sweetness, a tendency to overwork which might prove dangerous.

Chappuis quotes part of a letter written during the time when Pasteur was pursuing his crystallographic researches :

" I am approaching mysteries, and the veil which covers them is gradually diminishing. Also the nights seem too long. All the same I do not complain, for I have five whole days each week to devote to the laboratory ; but I am often scolded by Mme Pasteur, whom I comfort by telling that I am making her a name which will be known to posterity."

The 29th of May was a lucky date. Mme Pasteur was to make a happy home for her husband, and to spare him throughout a long life all such material worries as might distract him from the scientific investigations which he pursued with such ardour and with such success. She well deserved this tribute, rendered by one of Pasteur's dearest disciples : " She was not only an incomparable companion to her husband, but also his best collaborator."

CHAPTER IV

FURTHER STUDIES ON CRYSTALLOGRAPHY

WITHOUT interruption Pasteur followed up the researches in crystallography which had already obtained for him valuable encouragement from those members of the Academy of Science—Dumas, Biot, and Senarmont—to whom he had presented his results.

He had a keen desire for a better understanding of paratartaric acid, the object of one of his earliest investigations, which had so far only been obtained by accident, in an uncertain manner, during the treatment of crude tartars. He learnt that a certain Leipzig manufacturer had succeeded in producing it. Immediately he dashed off in search of him, with the ardour of a policeman on the track of a criminal. He thus employed his vacations during the year 1852, but without obtaining any light on the question which so excited his interest from any of the chemists whom he interrogated.

At last, in the month of May 1853, he succeeded in transforming tartaric acid into paratartaric. Biot, Senarmont, and Pasteur himself had believed this to be impossible. It must, they said, have incalculable consequences. Its first effect was that of gaining for its author the Cross of Chevalier of the Legion of Honour, and a prize of fifteen hundred francs awarded by the Pharmaceutical Society of Paris.

This sum enabled Pasteur to supply some of the deficiencies in the collection of apparatus in his laboratory. He then made an interesting experiment. He fractured a crystal at one of its angles, and afterwards replaced it in the mother-liquor. The crystal developed symmetrically on all its surfaces, but the deposition of crystalline particles was especially active in the neighbourhood of the injury, so that after a few hours the crystal had regained its normal shape. As Pasteur pointed out, it is impossible not to compare this phenomenon with the process of healing in a wound.

These discoveries, which interested Biot and certain of his colleagues intensely, did not meet with admiration only. Joseph Bertrand has reported an observation made to him on the subject of hemihedral facets : " Why so much fuss about little facets hardly visible under a magnifying-glass ? Whether they exist or whether they don't, whether they turn to the right or the left, what does it matter to me ? " and Bertrand added : " One of M. Pasteur's most ingenious experiments allowed the answer : microbes are more inquisitive than you are ; the position of the facets is not a matter of indifference to them, they either treat with respect or else destroy the crystals which bear them, in accordance with the result of the analysis they make, quite as successfully as M. Pasteur himself, who is proud to be in agreement with them."

Pasteur had demonstrated to Biot that paratartaric acid is without action on polarized light because it consists of a mixture in equal parts of dextro and lævo tartaric acid, which have an action on this light in opposite directions. Moreover, solutions of tartaric acid can undergo fermentation, they can afford nourishment to certain organisms, and know how, in a solution containing both, to choose the one they prefer. Thus *penicillium glaucum*, the very common mould which develops in the form of a greenish moss on the surface of damaged fruits, grows readily in a liquid containing paratartaric acid. Pasteur has proved that this little plant consumes exclusively the acid which deviates polarized light to the right, whereas it leaves the lævo acid untouched until it has no more of the dextro acid at its disposal. The proof of this is easy : the solution of paratartaric acid is *indifferent* ; when the penicillium has consumed a certain quantity of the dextro acid, the rotatory power of a corresponding quantity of lævo acid is at once shown by the deviation of the plane of polarization to the left.

Senarmont has given, before his colleagues of the Academy of Science, an excellent exposition of the value and interest of this series of studies:

"M. Pasteur carries out, to begin with, prolonged and minute experimental researches in crystallography, which permit him to define those quite peculiar and formerly absolutely unknown conditional circumstances which connect to a measurable optical property, to the rotatory power of the molecule, and in consequence to the internal structure of the substance, the geometrical peculiarities of their crystalline envelope.

"Thus equipped with a double method of investigation, the laws of which he has just discovered, he demonstrates an absolutely unexpected fact, namely the existence of certain substances chemically identical, but differing, since both optical and crystallographical character bear witness equally to a molecular arrangement symmetrically inverse.

"By a perfectly rational induction he infers from the dual existence of these substances that, in all phenomena in which he shall succeed in making them take part, it will be possible for him to distinguish the part purely chemical and due to the nature only of the molecules, since this must be the same in the two cases, from the part purely mechanical, due on the other hand to their arrangement, since in the two cases it must be absolutely opposed.

"The same principles of induction aid him to foresee and determine in advance to what specific substance he must associate by combination the peculiar bodies the presence of which he has demonstrated, sometimes to permit the simultaneous existence of the chemical entity and the opposite molecular arrangement with the geometrical peculiarities which characterize it; sometimes to produce a complete transformation of all properties at once, by changing at a blow both chemical composition and internal structure.

"Not only has M. Pasteur drawn all these logical deductions from his crystallographic researches, but he has, everywhere and always, known how to confirm them by an equal number of decisive experimental proofs.

He has understood how to rise continually and with equal success from the theoretical conception which imagines to the experiment which demonstrates, and from the demonstration itself to fresh speculative conceptions; with the result that logical induction and material observation serve each other in turn, and in a continuous series, as corollary and verification."

These works of Pasteur on crystalline dyssymmetries inspired the investigations of Le Bel and Van't Hoff, which were to result in their beautiful conception of stereo-chemistry, and, by explaining the structure of many organic compounds, to enable innumerable syntheses to be foreseen and realized.

CHAPTER V

PASTEUR DEAN OF THE FACULTY OF SCIENCE AT LILLE—FERMENTATIONS—LACTIC FERMENTATION

PASTEUR's growing reputation led to his nomination in September 1854 as Professor and Dean of the recently created Faculty of Science at Lille.

Permission had recently been granted to the pupils of Science Faculties to carry out practical work in the laboratories, and at his first lecture the young Dean wisely pointed out to his audience the advantage they would obtain from this innovation. "What young man is there," he said, "whose curiosity and interest will not be immediately aroused when one puts into his hands a potato from which he can obtain sugar, from that alcohol, and from the alcohol either ether or vinegar.

"Work done in this way is seldom or never forgotten. It is much the same as if a pupil were taught the geography of a country by travelling in it. Geography so learnt is impressed upon the memory, because one has seen and been in actual contact with the places."

In this industrially important district, where theoretic work was little appreciated, and only positive results valued, Pasteur aroused minds to more lofty conceptions; he said to his pupils: "Without theory practice is but the routine of habit. Theory alone can awaken and develop the spirit of invention. It is essential that you especially should not share the view of those limited intellects which despise all science which has no immediate practical application. You know the delightful saying of Franklin. He was assisting at the first demonstration of a purely scientific discovery. One of the bystanders asked him: "But what is the use of this?" Franklin answered: "What is the use of a new-born child?" A theory has only one merit, that of existence. It awakens hope, that is all. But tend it, let it grow, and you will see what it will become.

"Do you realize the moment at which the electric telegraph first saw the light? It was in the memorable year 1822. Œrsted, a Danish physicist, was holding in his hands a copper wire connected to the terminals of a voltaic pile. On his table there chanced to be a magnetic needle suspended on a pivot, and he saw (you may say by accident, but do not forget that in the field of observation chance favours only the trained mind) the needle suddenly assume a different position to that taken up under the force of terrestrial magnetism. A wire through which an electric current passes alters the position of a magnetic needle. That was the actual birth of the telegraph. With how much more reason, when he saw the needle move, might not Franklin's interrogator have said: 'But what is the use of this?'"

Pasteur already understood from his own experience the profound truth of these words: "In the field of observation chance favours only the trained mind."

He made a most conscientious professor, shirking no toil in order to make his lessons clearer and more interesting, to base them on convincing experiments, and increase their utility. In consequence the little amphitheatre where he delivered his course of lectures soon became too small.

The father of one of his pupils came to him to explain the difficulties which he was encountering in the manufacture of alcohol from beetroot; sometimes for some inexplicable reason the process, to all appearance excellently carried through, turned out badly; he did not see how chemistry could get him out of his difficulty, but he had confidence in the chemist's talents. Pasteur did not hesitate, but attacked the difficult problem of fermentation.

The question was then in a confused state, full of contradictions, obscurities, and errors. The phenomena of fermentation have been known since the beginning of time. How can one fail to notice the bubbling which appears in grape-juice when left to itself, and the change which follows? Our prehistoric ancestors knew how to make wine, though no doubt the ways of making bread and beer were discoveries of rather later date. The French words *levain* and *levure,* leaven and yeast, are almost the same. Yeast is the froth which rises to the surface in barrels of beer, and then sinks to form a deposit at the bottom. It rapidly increases in amount when planted in a sugar-containing wort, and appears to develop spontaneously when not sown. This increase of yeast accompanies the fermentation of the wort, so that one cannot fail to recognize a relationship of cause and effect between these two phenomena: it is the yeast which is the ferment.

The doctrine universally accepted before Pasteur regarded fermentation as a purely chemical process. The yeast was regarded as a nitrogenous material of ill-defined composition, related to gluten, which, like other organic substances, is destroyed by putrefaction. Liebig, adopting the ideas already expressed by Stahl at the end of the seventeenth century, said: "Beer-yeast, and in general all other animal and vegetable matters in a state of putrefaction, convey to other bodies the state of decomposition in which they are themselves. The change which, by the disturbance of equilibrium, takes place in their elements, is transmitted also to the elements of bodies with which they come in contact." This was a purely mental conception, accepted without demonstration; it is necessary to seek a better explanation. The statement, however, that the commonest fermentations (alcoholic, lactic, and butyric) could be produced by introducing into fermentable material old cheese, bad wine, or any substances whatsoever which were in a state of decomposition was justifiable.

Now Leeuwenhoeck had observed in 1689 that yeast examined under the microscope appeared to be made up of ovoid globules, apparently organized. In 1835 Cagniard de la Tour made the same observation; he recognized that yeast was a mass of globules capable of reproduction by budding, and not a simple organic or chemical substance as was supposed; and he concluded: "It is very probable that, as a result of their growth, the yeast globules set free carbonic acid from the sugar-containing fluid, and change this into spirit-containing liquor." Schwann at the same period recognized in yeast a vegetable germ which, feeding on the sugar rejects, in the form of alcohol, the part of which it cannot make use.

These views, however, based on insufficient and not always successful experiments, had not carried conviction. Chemistry, proud of its great advances, reigned then supreme; for Liebig and his pupils the introduction of vital forces into a domain where chemical analysis by itself was capable of giving a complete explanation was a mistaken and retrograde proceeding.

Berzelius was ready to see in fermentation nothing but an action of contact, and said about the cells described by Cagniard de la Tour that: "They were merely a chemical product, a precipitate formed during the fermentation of beer, and that they took the normal shape of non-crystalline precipitates even of an inorganic nature, namely, that of little balls arranged one after the other like chains of beads." He added also: "When dissolved matters are precipitated it is quite natural for them to imitate the simplest forms of vegetable life. Form alone is not that which constitutes life."

Pasteur determined to study all the phases in the manufacture of alcohol. He followed out minutely the fermentation of beet-juice; with the simple means at his disposal in his poor laboratory, he examined the globules of Leeuwenhoeck and Cagniard de la Tour, and made many attempts to discover the secret law of their development. He was often deceived: the experiment of one day ruined the hypothesis of the day before, without lessening his enthusiasm for his researches. One day he noticed that the yeast-globules were rounded in a true alcoholic fermentation, but that they became longer and longer when the change dreaded by the manufacturers occurred, and that the fermentation became lactic; this observation was a notable advance, because in itself it provided a useful means of keeping an eye upon the manufacture of alcohol.

His studies on rotatory power inclined Pasteur to believe that, contrary to the opinions of Liebig, fermentation is the result of a vital process.

Amyl-alcohol is obtained specially by the fermentation of potato-starch; but is met as a secondary product in many other fermentations, and particularly in those which produce lactic acid. It deviates the plane of polarized light to the left, and this is easily explained by Liebig's theory: fermentation being a decomposition, the molecule of amyl-alcohol ought to possess the rotatory power of the sugar from which it is obtained.

Pasteur said, however, in the preface of his *Treatise on the Fermentation known as Lactic*: "Whenever one tries to trace the rotatory power of a substance into its derivatives, one finds that it immediately disappears. The original molecular grouping must remain almost unaltered in the derivative if the latter is to remain active, a result which my researches allowed me to foresee, since the optical property is entirely a matter of dyssymmetrical arrangement of atoms."

Pasteur was convinced that life only is capable of creating new dyssymetries; the admission therefore seemed to him logical that the fermentation which produces amyl-alcohol is a phenomenon of a vital order.

Liebig avoided a verdict on the organization of the yeast-globule. What did it matter whether the yeast was a living thing when it only acted after death as all other organic matter during decomposition? No doubt it could always be seen in alcoholic fermentation, but took no part in other analogous fermentations, such as the lactic, where it is never met with. Is this not a proof of the insignificance of its rôle? What a much simpler and more certain doctrine is that which rejected this hypothesis of cellular life, and explains all fermentation with one formula only!

Pasteur interrupted his researches on alcoholic fermentation in order to find out whether lactic fermentation occurred without the intervention of a yeast.

It was known that this latter fermentation ceases when the medium becomes acid, but by adding chalk to the sugar solution, with the object of maintaining its neutrality, and some nitrogenous substance, such as old cheese, decomposed gluten fibrin, albumen or other decomposing organic matter, the sugar is transformed into lactic acid, which becomes, by combination with the chalk, calcium lactate. The débris of these organic materials formed at the bottom of the vessel more or less compact deposits, differing widely in appearance, the elements of which it was difficult and also almost useless to identify. Pasteur, however, with his observant and clear-sighted eyes perceived in some cases streaks of the grey substance formed in the upper part of the deposit spread over its surface. This substance, when examined under the microscope, was found to be composed of little cellules, constricted in the middle like an 8, and presenting an organized appearance, but much more difficult to recognize than the globules of beer-yeast, whence no one up till then had observed them. Often, in fact, these globules appeared in a "mass consisting of irregular flakes similar to those of certain amorphous precipitates."

Pasteur thought that organic matter was only of use in nourishing the ferment, so to obtain a clearer view of his experiments, instead of provoking fermentation with old cheese and other material, which made the liquid turbid and caused the deposits to adhere together, he set to work with only carefully filtered and clear infusions, which enabled him to obtain a deposit formed entirely of the grey substance which he took to be the yeast of lactic fermentation. An imperceptible trace of this, transported to a new solution suitably prepared, set up a fresh fermentation, in all points comparable to the first, and this process could be continued indefinitely by successive sowings.

It is not without interest to note that this operation of sowing, from which Pasteur obtained such wonderful results, was first performed in the course of his investigations on lactic fermentation. It is enough to touch the veil of yeast with the fine tip of a glass rod—some cellules will adhere to the point, and this infinitesimal quantity of seed suffices to set up fermentation.

Pasteur concluded from his experiments " that fermentation is thus shown to be correlated to the life and formation of the globules, and not to their death or putrefaction; furthermore, it is not a phenomenon appearing as a result of contact, where transformation of the sugar takes place in the presence of the ferment without giving anything to it or taking anything away."

This was an explicit refutation of the doctrines of Liebig and Berzelius.

In this first memorandum Pasteur has pointed out well supported facts, which are of great importance, and which must be kept in mind:

" If one sows beer and not lactic-yeast in an albuminous and clear solution of sugar, it is the beer-yeast which will develop, and with it an alcoholic fermentation, so long as the other conditions of the operation are unchanged. One should not conclude from this that the two yeasts have an identical chemical composition, any more than that that of two vegetables is the same because they have grown in the same soil.

" It is not essential to have lactic-yeast already in order to prepare it, it develops spontaneously with the same facility as beer-yeast whenever conditions are favourable."

Pasteur notes also that he uses the word *spontaneously* to express the fact, without committing himself on the question of spontaneous generation. This assertion is, finally, of the greatest importance, it will transform the whole industry, and bring about a tremendous advance.

" The purity of a ferment, its homogeneity and free development without hindrance, by the aid of nourishment well adapted to its individual nature, is one of the essential conditions of successful fermentations."

Pasteur was to add later that the chief difficulty of studies in fermentation consists in producing the different ferments in an individual isolated state.

“I can bear witness,” he says, “to the existence of a large number of distinct yeasts, setting up various chemical transformations in accordance with their nature and constitution; but most frequently the nourishment best suited to one allows others to develop. Hence arise most complicated phenomena, liable to constant variation. If one does succeed in separating one of these ferments and making it grow by itself, it produces the corresponding chemical change with remarkable precision and simplicity.”

CHAPTER VI

PASTEUR AT THE ÉCOLE NORMALE—ALCOHOLIC FERMENTATION

During the three years in which he held his professorship Pasteur had served Lille and its new Faculty of Science with distinction. He was of opinion, however, that he could be more useful elsewhere. His beloved École Normale had sunk at this time into a state of complete decadence; he longed to assist it to recover, and hailed his nomination in 1857 as Administrator of the school and Sub-Director of Science-Studies with delight.

His administrative functions included the care of hygiene and diet, by no means the sort of work to which he had been accustomed. Pasteur, however, was too deeply conscientious to neglect any duty; he interested himself in the feeding of the pupils and the up-keep of the buildings with that same care which he bestowed on his laboratory research work.

The École Normale had no laboratories except for the use of the students and the professors employed for their instruction; Pasteur arranged one at his own expense in the corner of a loft; it consisted of two rooms, ice-cold in winter and so unbearably hot in summer that work became impossible. It was there, nevertheless, that he followed up his investigation of alcoholic fermentation.

The chemical side of this problem had been solved by Lavoisier. He had added a little beer-yeast to a definite quantity of sugar and water, mixed in exact proportions. He had collected and weighed the carbonic acid liberated during fermentation, and determined that the solution had undergone a corresponding change in weight. He obtained by distillation the alcohol formed in the liquid, and found that the combined weights of the alcohol and carbonic acid gas almost exactly equalled that of the sugar employed. Lavoisier has summed up the results of his experiment with absolute clearness thus:

"The effects of vinous fermentation consist of a separation into two parts of the sugar, which is an oxide; in oxidizing one of these at the expense of the other so as to form carbonic acid; and in deoxygenating the second by the help of the first so as to form a combustible substance—alcohol; with the result that, if one could recombine these two substances, alcohol and carbonic acid, one could reconvert them into sugar."

This clear demonstration convinced everybody. In spite of this, however, the inefficiency of the analytic methods of the time prevented Lavoisier from determining the exact composition of sugar and alcohol, and his conclusions are only correct, as Pasteur has pointed out, thanks to the fact that by good luck his errors compensated one another. It should be remarked, too, that these conclusions ignore the beer-yeast, without which there could be no fermentation.

In his treatise on alcoholic fermentation, Pasteur established a whole series of new facts. He proves that this fermentation does not stop short at splitting the sugar into carbonic acid and alcohol. It invariably produces glycerine and succinic acid, the elements of which are obtained from the sugar, not the yeast. Besides this it is from the sugar that the yeast gets part of the material of which it forms its globules.

As a result of badly carried out and falsely interpreted experiments, Doebereiner, a German chemist, had discovered in fermented liquor ammonia, whose origin he attributed to a partial destruction of the yeast. Because organic matter during decomposition gives off ammonia, Liebig seized on these results to form a basis for his theory. Pasteur shows that on the contrary if one adds ammonia to the liquor, the yeast takes nitrogen from it, and combines it as albuminous matter in the substance of its own globules.

Finally, to decide the matter definitely, Pasteur undertook to cultivate yeast in a medium into which no particle of nitrogenous organic matter was introduced and without which Berzelius and Liebig imagined fermentation impossible.

The problem was difficult. Yeast has a very complex composition, it finds in the organic matter usually submitted to it, such as grape-juice, or beer-wort, a certain number of directly assimilable materials; if it were forced to prepare the materials by means of elements obtained from chemically pure mineral salts, it is doubtful whether it would be capable of so formidable a work of organization.

Pasteur prepared a liquid containing only pure water, sugar, mineral phosphates and a salt of ammonia; and in this medium, from which all nitrogenous organic material was excluded, he sowed an imperceptible trace of yeast. Fermentation was set up, and the yeast grew. This experiment was decisive.

Pasteur could affirm after this that: "sugar never undergoes alcoholic fermentation unless some globules of yeast are present and alive, and on the other hand the beer-yeast only forms globules in the presence of sugar or hydro-carbons, and when these undergo fermentation."

He ended by triumphantly repeating the conclusion of his first account: "alcoholic fermentation is essentially a vital process, connected with the growth and not the death or decomposition of certain globules, nor did it appear as a phenomenon of the contact when the transformation of the sugar took place in presence of the ferment without either giving or receiving anything from it."

CHAPTER VII

BUTYRIC FERMENTATION—AEROBES AND ANAEROBES—PUTREFACTION

FROM now onwards, Pasteur, possessed of a method which obviated old sources of error, revised his early experiments ; he successfully cultivated in the same artificial medium which contained no organized nitrogenous matter, the lactic ferment, then the butyric. The latter had a great surprise in store for him.

Every time that he examined under the microscope a drop of fluid in which butyric fermentation, so called because it occurs when butter has become rancid, had been set up, he saw only minute mobile rods, sometimes separate, at other times united in chains of two or more individuals. These little rods move in a gliding manner. When in chains one can often notice that an individual leading a chain of others wriggles about in order to free itself, which it actually succeeds in doing, multiplying itself by thus dividing into two, or as we may say by *fission.*

Pasteur called the little rods *vibrions*, and as they resembled those entities which the naturalist Dujardin had observed in infusions, he classed them among the Infusoria, and because, at that time, movement appeared to be a power possessed only by members of the animal-kingdom, he thought that these vibrions must be of animal nature. The non-mobile globules of alcoholic and lactic ferments belonged incontestably to the vegetable kingdom. This difference in the nature of organisms which had functions and properties so similar, troubled Pasteur considerably, but he was too much under the influence of experimental results not to recognize the fermenting property of this vibrion, without whose presence no butyric fermentation could be set up. This ferment, already so clearly distinguished by its shape, showed a peculiarity of quite different importance: it could not live in contact with air. Pasteur was always ready to describe the way in which he was led to make this discovery.

In order to examine the fermented liquor, he had placed a drop on a glass slide, spread this drop by pressing it out under a cover-slip, and then observed under the microscope that the vibrions, very active at the centre of the slip, where air could not penetrate, lost all their mobility at the edges. The animalcules from infusions, which are true infusoria, behave quite differently; they are seen to seek the edges of the cover-slip. These margins are permeated with oxygen; was it not the presence or absence of this gas which explained the different behaviour of the infusoria and vibrions? Pasteur, to satisfy himself of this, passed a current of air into a liquid in active butyric fermentation,—the vibrions perished, and the fermentation ceased; but if he passed a current of carbonic acid gas into the liquid, the life and reproduction of the vibrions were not in any way interfered with, and the fermentation depending on their life continued.

This, Pasteur said, was the first example known of animal ferments, and at the same time of animals living without free oxygen; later he was to create the words *aerobic,* to describe life in contact with air, and *anaerobic* to signify that without air.

Oxygen, however, is everywhere in air mixed with other things, and in water in a state of solution. How then can anaerobes develop in an infusion? Pasteur immediately solved this problem. The newly prepared infusion contains aerobic organisms which absorb the dissolved oxygen; they then disappear from a medium become unfitted for their existence, but from now onwards adapted to that of the butyric vibrion. On the surface of the liquid, which is in contact with the air, aerobes continue to exist, they absorb the oxygen and prevent it from penetrating further than the superficial layer, where they multiply, and so allow the anaerobes to develop in the deeper parts.

This conception of two simultaneous existences, one protecting the other, was to lead Pasteur to show how: "dead matter which ferments or putrefies is not obedient, at any rate exclusively, to forces of a nature purely physical or chemical. It is life which rules over the work of death, and the dissolution of animal and vegetable matter. "This constant return to the atmospheric air and to the mineral kingdom of the constituents which vegetables and animals have borrowed from them, is an act related to the development and multiplication of organized beings."

When an animal dies, the whole surface of its body is covered with dust and germs from the air. The intestinal canal is filled not only with germs but with fully developed vibrions, arrived at the adult state in a medium where they are protected from oxygen and where they find the elements necessary for their nutrition. The life of the animal alone prevents their surmounting the barrier presented by the intestinal wall; as soon as respiration ceases, the blood can no longer be oxygenated and carry oxygen to all the tissues, and the barrier breaks down; the vibrions then invade the dead body and putrefaction will begin.

The vibrions being without air bring about the process of fermentation, that is to say they change nitrogenous organic matter into more simple but still complex products. It becomes the function of aerobic organisms to seize on these products, to consume them with the help of oxygen, and reduce them to more simple compounds, such as ammonia, water, and carbonic acid. So putrefaction in contact with air is always more complex than that which takes place in a situation to which air is denied access.[1]

The Academy of Science had recognized the great importance of Pasteur's work on fermentation by awarding him, on January 30, 1860, the prize for experimental physiology.

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[1] Pasteur will be found returning to this question when Biot asks him at the Academy of Medicine: "What are the ferments which act upon ferments?" See later, p. 145.

CHAPTER VIII

SPONTANEOUS GENERATION

1. Up to the time of Pasteur.

In a note presented to the Academy of Science, May 7, 1860, Pasteur said: "Among the questions raised by the researches which I have undertaken on what are rightly called fermentations, none is more worthy of attention than that concerning the origin of ferments. Whence come these mysterious agents, so weak in appearance, so powerful in reality, which, of the lightest possible weight, with insignificant external chemical characteristics, possess exceptional power? This is the problem which has led me to the study of spontaneous generation."

This question, constantly discussed and never solved, divided for centuries wise men and philosophers. Almost all the ancients believed in spontaneous generation or, as they call it, *heterogenesis*, that is to say in the birth of beings without antecedents similar to themselves. Lucretius said, in fine verse: "even now there come out of the ground animals which are brought forth by the rain or the warm exhalations of the sun," and Vergil prescribed the following method for obtaining bees: "Kill an ox two years of age, whose young horns are just beginning to curl upon his brow, place him in a narrow enclosure strewed with leaves of thyme and rosemary freshly gathered, and soon from his fermenting humours there rises a swarm, which fills the air like rain from summer clouds." Many authors, even as late as the seventeenth century, described the way in which frogs could be produced from the slime of marshes, or eels from river-water, and Van Helmont, who had a great reputation for wisdom, gave a recipe for procuring rats: "all that is required is to cork up a pot containing corn with a dirty shirt; after about twenty-one days a ferment coming from the dirty shirt combines with the effluvium from the wheat, the grains of which are turned into rats, not minute and puny, but vigorous and full of activity." The worms which appear in bad meat were cited as an example of spontaneous generation.

In spite of these beliefs there occurred to Redi, an Italian naturalist, the idea of putting a piece of fresh meat under a gauze covering; the flies, not being able to get at the meat, alighted on the gauze, deposited their eggs there, and the worms hatched out of them; therefore the statement that these worms were the product of spontaneous generation could no longer be made. This was a confirmation of Harvey's aphorism: *omne vivum ex ovo*, a saying which in the opinion of its originator did not hold good absolutely, for Harvey himself believed in heterogenesis, and after having said "Every living being comes from an egg," he added, "or from the dissolved elements of anterior life."

The doctrine, rendered suspect by Redi's observation, found new supporters when the invention of the microscope allowed it to be seen that although worms did not appear in meat protected by gauze, the meat none the less putrefies, and swarms with innumerable organisms invisible to the naked eye.

The question continued a matter of philosophical dispute up to about the middle of the eighteenth century, when Needham, an English Catholic priest, published a book in which he affirmed the truth of spontaneous generation, relying on experiments of quite a fresh nature. He had quite understood that the germs to which the adversaries of spontaneous generation attributed, though without proof, the birth of those microscopic organisms which develop in matter liable to putrefaction, can exist beforehand on these materials, or on the sides of vessels which contain them, or may float in the surrounding air. It occurred to him to close the vessels and submit container and contents to the action of heat, with the object of destroying the germs which would have developed in an experiment not carried so far. If, in spite of this procedure, living organisms developed in the material after cooking, they could only have been produced by spontaneous generation.

Needham buried well-stopped flagons containing different vegetable infusions beneath hot cinders. Some days later all the infusions had become turbid, and all contained organisms visible either to the naked eye or under the microscope. This appeared to the observer to mean a new creation. These results were rather disturbing to a Catholic priest, who asked himself if they could be reconciled with his faith. He wrote a dissertation to convince himself and others that spontaneous generation was not incompatible with his religious convictions.

Buffon adopted Needham's ideas, and relying on them, built up a wondrous theory. When an animal dies it does not die in its entirety; "the matter of living beings preserves after death some of its vitality. The life is contained essentially in the last molecules of the body; . . . these always active organic molecules try to move the putrefying matter; they appropriate to themselves some particles, and form by this union a multitude of little organized bodies, of which some, such as earthworms, toadstools, etc., seem to be fairly large animals or vegetables, but others, which are almost innumerable, can only be seen through a microscope. All these bodies only exist by spontaneous generation, and they fill the gap which nature has made between the single living organic molecule and the animal or vegetable; thus one finds every degree and every imaginable variety in this series, in this chain of beings which descends from the organized animal to the simple molecule of organic matter." This conception was deficient not so much in magnificence as in everything of the nature of truth.

In 1765 the Abbé Spallanzani, a very accomplished Italian physiologist, published a criticism of Needham's experiments. He was of opinion that the English scientist had not submitted his flagons to a sufficiently high temperature, and that his corks did not close them efficiently. He made fresh experiments which gave quite different results. Needham protested: "Spallanzani," he said, "hermetically sealed nineteen vessels filled with different vegetable substances, and boiled them, thus closed, for an hour; but he has treated and tortured these nineteen vegetable infusions in such a way that he has plainly not only greatly enfeebled them and possibly entirely destroyed the vegetative force of the infusions, but also has corrupted the small amount of air remaining in the empty part of his phials by the fumes given off and by the heat of the fire. It is not surprising that infusions so treated should no longer show evidence of vitality."

The "vegetative force" of an infusion is merely a form of words and has no more value than the "dormitive virtue" of opium which Molière had derided in the previous century. Spallanzani said: "You do not heat sufficiently"; Needham replied: "You heat too much, and, besides, you pollute the air." It was impossible to refute this last argument because at that time the composition of air was unknown. The question therefore remained unsettled.

Spallanzani's ingenious experiments were, however, not destined to remain useless. One of them had consisted in the introduction of green peas and water into a closed and hermetically sealed glass vessel, which was then kept in boiling water for three quarters of an hour. The peas thus treated remained indefinitely unaltered.

Appert employed the same procedure and devised the method known by his name for the manufacture of preserved food-stuffs.

A little later Gay-Lussac analysed the air contained in one of Appert's flagons and found that the oxygen had disappeared. Thus Needham had not been wrong when he accused Spallanzani of corrupting and upsetting the air in his vessels. Gay-Lussac came to the conclusion that the absence of air was a condition necessary to the preservation of animal or vegetable substances. This was saying more than the results of his analysis justified; in fact different experimenters were to show that the contents of Appert's flasks remained unaltered when air which had passed through strong sulphuric acid reached them,[1] or which had been heated by passing through a bath of fusible metal,[2] or been simply filtered through a sufficient thickness of cotton.[3]

It seems that these experiments ought to have solved the problem; but they did not succeed with certainty with ordinary infusions, and they never succeeded with macerated meat, albumen or yolk of egg. Schroeder wrote in 1859: "One might admit that fresh air contains an active substance which induces the phenomenon of alcoholic fermentation and putrefaction, a substance destroyed by heat, or kept out by cotton. Is this active substance to be regarded as consisting of organized microscopic germs disseminated through the air, or rather as a chemical substance still undiscovered? I know not."

In December 1858, Pouchet, Director of the Natural History Museum at Rouen, had just communicated to the Academy of Science results which seemed to him to furnish a convincing demonstration of heterogenesis.

Therefore in 1859 the Academy, with the desire of clearing up this question which was absorbing the scientists, and even the general public, of the whole world more and more, offered a prize for: "An endeavour by means of careful experiments to throw new light on the question of spontaneous generation." The Committee appointed to judge the work of the competitors consisted of Geoffrey Saint-Hilaire, Brogniart, Milne-Edwards and Flourens. They demanded: "Well-defined experiments, conducted with every precaution, studied with regard to every condition affecting them; in short, experiments from which can be deduced results freed from the confusion created by the experiments themselves."

Pasteur was prepared by his studies in fermentation for this demand for fresh investigations, but the friends and masters dearest to him were not pleased to see him engaged in this way. Biot, who showed a fatherly affection for him, was particularly upset; he did not wish Pasteur to attack a problem which he himself judged insoluble, and begged Pasteur that at least, in deference to his wishes, he would abandon the subject after a definitely limited time if he had not up till then been able to master the difficulties which confronted him. J. B. Dumas, likewise consulted, was by no means encouraging. He said: "I should not advise anyone to devote much time to such a subject."

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[1] Schultze, 1836.
[2] Schwann, 1837.
[3] Schroeder and Dusch, 1854.

2. The Laboratory of the École Normale. The Germs of the Air.

In the entrance court of the École Normale, a little lodge, corresponding to that occupied by the porter, bears a small tablet with the following inscription:

THE LABORATORY OF
PASTEUR
SET UP IN AN ATTIC
1857
WAS ESTABLISHED IN THIS LODGE
1860
ENLARGED BY THE ADDITION OF THE ADJOINING BUILDINGS
1862–1869.

Another marble slab has been affixed, by the city of Paris, to the front of the adjacent building facing the Rue d'Ulm:

HERE WAS
THE LABORATORY
OF
PASTEUR
1857
FERMENTATIONS
1860
SPONTANEOUS GENERATION
1865
DISEASES OF WINE AND BEER

1868

DISEASES OF SILK-WORMS

1881

VIRUS AND VACCINES

1885

PROPHYLAXIS AGAINST RABIES

These dates mark the principal stages of a glorious life.

At the same time as these premises were made more suitable to the use for which they were destined, Pasteur obtained an assistant. He had decided to create five appointments of this kind for pupils of the École Normale who had taken their degrees. These *agrégés* could thus complete their studies and do original work while remaining in close touch with their instructors. Pasteur's first assistant was Jules Raulin, who possessed an original mind, was a patient and clever experimenter, and one who was to show himself capable of successfully undertaking the most delicate researches.

After Raulin came Duclaux, who has mischievously recalled the difficulties Pasteur had to surmount in overcoming administrative " red-tape " : " Plenty of assistants were provided for by the budget of the École Normale, but, like the laboratories, they were only for the use of students, and I fancy M. Pasteur must have excited some astonishment and distrust when he asked for an assistant especially for himself. I have evidence of this in the delightful form in which the first agreements for the appointments were drawn up. Mine is in these terms : I am ' authorized to remain attached to the Laboratory of the Director of Scientific Studies, it being understood that if in the course of the year the exigencies of the service require that M. Duclaux be sent to one of the schools of the departments, he must place himself at the disposal of the Administration. This is the only condition on which the Administration can permit him to remain at the school.' In spite of all this I was housed and fed there and received fr. 47.50 a month."

No grant was allowed the laboratory. The Minister of Public Instruction replied to a request from Pasteur :

"There is no heading under Expenditure which will permit me to allow you even fifty centimes towards the cost of experimental work."

The result was that Pasteur supplied from his own pocket what the State Budget failed to provide.

As early as February 6, 1860, Pasteur communicated to the Academy of Science his *Experiments relating to Spontaneous Generation.* To satisfy himself as to the number and nature of the germs which might be contained in the air, he had again used, while improving it, the method of filtering through cotton already employed for various purposes by different observers. By means of a hydraulic aspirator he drew air through a wad of cotton-wool where the dust was retained, the dust being sometimes so abundant that the wad appeared black. He afterwards broke up the cotton-wool in a mixture of alcohol and ether, washed the dust, and then examined it under the microscope. Under these conditions small bodies, whose structure shows them to be organized, are always to be seen.

Pasteur then prepared a watery solution of albumen and sugar, a fermentable fluid containing 10 per cent. of sugar and about one half per cent. of albuminous and mineral matter obtained from beer-yeast. He then drew out the neck of the glass capsule containing the fluid to a fine thread, boiled it for some minutes, and allowed air which had passed through a red-hot platinum tube to enter through the open narrowed neck. He closed the neck in a flame with a blowpipe, and the solution remained unchanged indefinitely. This was Spallanzani's experiment corrected to meet Needham's objections.

Pasteur took the capsule, broke the point of the neck and allowed a small piece of the cotton wad which had acted as a filter for the air, to fall into the fluid. By means of special arrangements he worked in heated air, and was careful to replace with heated air that which would ordinarily have been retained in the cotton fibres. In this way there comes in contact with the sterile liquid only air which has been heated and is therefore also sterile, and cotton with the dust left on it by the preceding experiment.

Germs identical with those which develop when the liquid is freely exposed to the air are found to appear in the capsule, so that what Needham would have called the *vegetative force* has not been destroyed. If one is afraid lest the cotton may be concerned owing to its vegetable nature, a wad of asbestos, previously made red-hot, can be substituted; this mineral wad, employed in the same manner as the cotton for filtering the air, will produce identical results.

Here at last is an experiment of the highest order and one that gives the mind that inner thrill which is felt in face of perfect work. Pasteur did not wish anyone to accuse him of destroying the air by the action of heat. He therefore took a number of capsules and filled them with fermentation fluid; elongated their necks in a flame, and bent them in different ways, particularly in the shape of a long swan's neck of very small diameter; he then boiled them for some minutes, except four which were kept as controls. These four, invaded by germs from the air, became turbid; the others underwent no alteration. The long curved necks, however, remained open in the case of all; and their mouths, which measured from one to two square millimetres of space, or a little more, were large enough, considering the relative dimensions, to allow germs to enter as easily as flies into a tunnel. As a result of the variations of temperature of the medium, the air is expelled when the temperature rises and returns on cooling, but these motions are made slowly, and the germs of the returning air are deposited on the still damp sides of the curves of the neck, and fail to reach the fluid. This can be proved in many ways. While the fluid is still boiling, close the fine extremity of the neck by applying a flame; a vacuum will be formed in the flask by the condensation of the aqueous vapour. Now break the neck. The air rushes back and its dust is drawn as far as the liquid, which soon shows alteration. Take one of the capsules, which for months or years has remained sterile by reason of its long neck, although in free communication with the atmosphere; close the neck, so that nothing can now enter; shake it violently, so that the fluid enters the curves of the neck, where the air has deposited its dust. By the next day you will see filaments which, radiating from points touched by the fluid, show that life has developed. One can also demonstrate the effect of the curves, by examining what happens in their absence: cut off the neck at the top of its vertical part; dust will enter by this small opening, and we shall soon see organized beings appearing in the capsule and generally even at the bottom of the vertical portion, entering by the opening of the neck.

In a fresh communication to the Academy of Science, dated May 7, 1860, Pasteur extends the results already obtained to the substances of milk and wine, which are more readily altered than fermentation fluid. Now if one is content simply with boiling the milk, it is found to undergo alteration almost as easily as the unboiled; this is because milk is alkaline, and in a medium with this reaction, germs are more resistant than in an acid or neutral one. It is necessary to heat milk to 110° C. or 112° C. under a pressure of one and a half atmospheres; then the germs are killed, and if their re-invasion is prevented, no alteration will occur in the milk. Another proof of the influence of the alkalinity of the liquid is given by fermentation fluid. When this is slightly acid, heating at 100° C. for two or three minutes is sufficient in order to sterilize it; if one makes it alkaline by adding a drop of calcium carbonate, it has, like milk, to be heated to 110° to 112°, to obtain the same result. This temperature of 110° to 112°, however, has not rendered the milk unsuited to the cultivation of germs, for all that is required in order to make the milk curdle and for the microscope to show various animal and vegetable organisms, is to introduce dust from the air. Pasteur could once more, and more forcibly, affirm that: "the ferment is not a dead substance, without definite properties. It is a living thing, the germ of which comes from the air."

Later Pasteur was to add that the fluids which are considered as most liable to alteration, blood and urine, taken with suitable precautions from the veins and bladder of living animals in perfect health, can be kept without alteration in contact with air, provided that this air is freed from germs. It is useless to submit them to any temperature, however high; the only way to protect them from germs seems to be to keep this blood and urine in the state in which they were taken from the living animal. After experimenting for a whole year, Pasteur proved that there is no putrefaction, the urine remaining unchanged even to its odour.

3. Unequal distribution of germs in the air.

On September 3, 1860, came a third communication to the Academy of Science:

"At the present time," says Pasteur, "everybody, both partisans and opponents of spontaneous generation, admits that the minutest quantity of ordinary air brought into contact with an infusion, will shortly determine there the presence of fungi or infusoria." Immediately the supporters of spontaneous generation hastened to point out, quite rightly, that if the smallest amount of ordinary air develops these organisms in any infusion, it necessarily follows, if organisms are not spontaneously generated, that in this small portion of air there must be the germs of a multitude of different growths; and in fact, if these things are so, common air must, as M. Pouchet observes, be loaded with organic matter, and would, according to M. Pouchet's estimate, form there a fog "as dense as iron."

All this was, however, mere talk, and not of as much value as the simplest experiment. "If this cause of spontaneous generation, this omnipresence of germs, cannot possibly be contained in the atmosphere," said Pasteur, "it simply does not exist at all. Let us try," and he immediately devised the concrete experiment which was to permit the solution of the problem.

He prepared a large number of capsules of about 250 cubic centimetres, filled about one-third full of the easily fermented fermentation fluid, which he generally used. He then drew their necks vertically upwards to a point, and boiled them for some minutes. Then by the application of a flame he closed the points while steam was still escaping, thus the liquid was sterilized and the flask emptied of air. One knows that under these conditions the liquid remains sterile indefinitely, but if one breaks off the point after the flask has cooled and the vapour condensed, the air returns with a rush; this is a neat and handy method of catching a small volume of air with all its contained germs. To make the experiment valid, no other germs must be added to these. Now germs are everywhere, on the clothes of the observer, on his hands, and on the point of the capsule itself. Pasteur took precautions to avoid these sources of error. He passed the neck of the capsule and its point through a flame, then raising it above his head, he broke the point with a pair of flamed pliers; the air whistled back and the broken point was immediately closed with a flame. The capsule was then placed in an incubator at 25° to 30° where it was under the best conditions for the development of the germs which had succeeded in getting in.

Pasteur took specimens of air in different parts of Paris, and in spite of the abundant dust, a certain number of capsules, as he had expected, remained sterile. A fixed temperature reigns all the year round in part of the cellars of the Observatory, the air is perfectly still, and must allow the dust which an occasional visitor may bring in soon to subside. It could be foreseen that the air of this cellar would give quite different results from that of the court-yard, and this was so. Of ten capsules opened in the cellar, one only changed; eleven were opened in the court-yard and the whole eleven showed alteration.

Following the same line of argument, the air should be purer and contain less dust the further one gets from inhabited districts and the higher one ascends a mountain, and it is conceivable that germs are almost completely absent in the region of eternal snow where all vegetation has disappeared. Pasteur opened twenty capsules in the country, some distance from any habitation, at the foot of the hills which form the first uplands of the Jura;

eight only underwent alteration. Of eight other capsules opened on one of the smaller mountains of the Jura, at a height of 850 metres, only five showed changes. Finally out of twenty opened on the Mer-de-Glace one only changed. Pasteur has related the history of these last.

He had kept thirty-three capsules for this final experiment. Arrived at the Mer-de-Glace he was disagreeably surprised to find that he was unable to close the first capsules by means of the blow-lamp which he was in the habit of using: "The whiteness of the ice under the sun's rays was such that I could not distinguish the flame from the burning alcohol, and the flame was also blown about somewhat by the wind, it never stayed long enough on the broken glass to melt the point and so hermetically seal the capsule. Any means then at my disposal which might have made the flame visible, and so easily directed, would have inevitably introduced causes of error by scattering imported dust into the air. I therefore was obliged to take the capsules opened on the glacier back to the little inn at Montanvert unclosed." These thirteen capsules remained thus open in Pasteur's room all night. Ten were invaded by infusoria or moulds. Meanwhile the lamp had been sent back to a tinsmith in Chamounix for the necessary alterations, and on the next day the twenty samples, of which nineteen showed no alteration, were taken.

Pasteur after this had every right to say: "I have established by numerous experiments that the cause of spontaneous generation is not universally present in the atmosphere; that is to say in a selected spot it is always possible to take a small but definite sample *which has undergone no chemical or physical alteration* and which is nevertheless incapable of producing any alteration in a liquid particularly liable to putrefaction." He was able to conclude: "If one brings together all the results which up till now I have obtained, one can affirm, so it appears to me, that the dust suspended in the air is the only origin and the first and essential condition of life in infusions." At the end of his communication Pasteur said, with regard to his researches: "It is very desirable to carry these researches sufficiently far to prepare the way for a serious enquiry into the origin of disease." This showed that already his mind was directed in a way which was to lead to so many wonderful discoveries.

4. Dispute with Pouchet.

Pasteur was not content merely with increasing the number of convincing experiments, he also pointed out the defects in those which might have been quoted against him.

Pouchet, in a communication to the Academy of Science in December, 1858, had loudly proclaimed his faith in spontaneous generation, and had pointed out in great detail those facts which appeared to him to demonstrate convincingly the truth of these generations. He had filled a flask with boiling water, corked it hermetically so that it contained not a bubble of air, inverted it over a bath of mercury, and when the water had cooled, introduced successively into the flask, oxygen and nitrogen, in the proportions necessary to form an atmosphere of artificial air, and then a small bunch of hay previously heated at 100 C. for twenty minutes. The hay infusion was at once filled with living germs. Whence came these germs? It could not be from the natural air, because the flask contained none at all; they were evidently formed by spontaneous generation.

"It is from the mercury that your germs come," answered Pasteur; "I will show you how the rats entered Van Helmont's pot. The mercury in a laboratory bath is constantly exposed to the dust from the air and always contains some. The special lightness of the dust particles would only bring them to the surface of the mercury if they were of a definite size. Besides if there were none at the bottom, if they were only on the surface of the mercury, it would still not be possible to avoid them during the operation. Spread some dust on the mercury and then plunge a glass tube into it. The dust seems to be attracted, and you see it collect by degrees in a sort of layer which forms between the glass and the mercury.

Sink the tube a decimetre or more, the dust will follow to this depth." Pasteur then gave a direct proof of his explanation. A globule of mercury taken from the laboratory bath and introduced into a fermentable liquid, always gives rise to organized growths, if one repeats the experiment under the same conditions, but if the mercury has been heated nothing grows.

In 1862 the Academy awarded Pasteur the prize it had offered to him who by well-constructed experiments should throw new light on the question of spontaneous generation. The committee was of the unanimous opinion that the experiments of Pasteur were such as they had demanded: "well defined, conducted with every precaution, studied with regard to every condition affecting them, in short, experiments from which can be deduced results freed from the confusion created by the experiments themselves."

Pouchet did not accept the success of his competitor without protest. He had written a whole book to explain the doctrine which he was trying to support with new force and authority. He said in the preface to his *Treatise on Heterogenesis*, published in 1859: "When after meditating on the question it became clear to me that spontaneous generation was still one of the means employed by nature to reproduce living beings, I set about finding means by which the phenomenon could be demonstrated." Pasteur had read this declaration of principles coming from a man of science who was entering upon experiments, not with the object of an impartial search for truth but to support a doctrine held as certain *a priori*, with stupefaction. It was like putting on, before looking, spectacles of the colour which one hoped to see. This state of mind is not really a very rare one. In a well-known encyclopedia, in the article on generation, published in 1872, these lines, which are even more astounding than the blind avowal of Pouchet, occur: "Spontaneous generation is no longer a mere hypothesis, it is a philosophic necessity. It alone is quite natural and alone frees us for the future from childish cosmogonies, driving off the stage that external and quite artificial *deus ex machina* which centuries of ignorance have worshipped." Behold then here, in an experimental science, a doctrine declared to be true by philosophic necessity, and one which is to free us from alleged puerile cosmogonies! Such declarations are so ingenuous that they disarm one. One can understand why Pasteur took as the text for one of his studies the words of Bossuet: "The worst disorder of the intellect is the tendency to believe things because one wishes them to be so."

Pouchet had found in Toulouse two zealous partisans, Joly and Musset, of whom the first, Professor of Zoology in the Faculty of Science, was of some repute. All three resolved to seek an experiment which would confute those of Pasteur. Pasteur had taken samples of air on the Mer-de-Glace at a height of 2,000 metres; they would take some on the Maladetta, 1,000 metres higher still! Actually they opened four capsules on the Recluse and four on the Maladetta in the crevasse of a glacier. They had the great satisfaction of seeing the eight capsules invaded by micro-organisms. Pouchet celebrated this victory in lyrical terms: "If M. Pasteur brought back sterile capsules from Montanvent, we, M. M. Joly, Musset and myself, after ascending to a much higher point in the Pyrenees, and as far as the glaciers of the Maladetta have returned bearing capsules full of animalculi. The peaks of Aragon, far higher and wilder than the ladies' favourite Mont Blanc, have given him the lie direct."

On the strength of this, the three heterogenesists accepted Pasteur's challenge, to take in any place whatever, with suitable precautions, a large number of samples of air, which would all, without exception, provoke the development of organized growths. Joly and Musset had written: "If but one of our capsules remains unchanged we will loyally acknowledge defeat"; and Pouchet: "I affirm that wherever on the face of the globe I shall take a cubic centimetre of air, no sooner shall I put it into contact with putrescible material enclosed in a hermetically sealed vessel, than this will invariably be filled with living organisms." The putrescible liquid which they used was not Pasteur's fermentation fluid, but an infusion of hay, filtered and boiled; this difference did not appear to be of any great importance.

First Joly and Musset, and afterwards Pouchet, demanded that the Academy of Science should nominate a committee before whom the principal experiments upon which the contradictory conclusions of both sides were based, should be repeated. Pasteur expressed the same desire. The committee was nominated; it included Flourens, Dumas, Brongniart, Milne-Edwards and Balard. The conditions of this remarkable duel seemed as well defined as possible. They had been clearly stated in the public declarations of the opponents.

The committee called upon the two sides to meet on March 15th, but Pouchet, Joly and Musset considered that the time of year would be unfavourable; they asked that the experiments should be repeated in the warm season. Pasteur remarked that it was easy with a stove to obtain whatever temperature was required; however, he held himself at the disposition of the Academy, ready to repeat his experiments in spring, summer or any season.

A new meeting was agreed on by both sides for June 15th. Pasteur had brought from the laboratory of the École Normale all the necessary material; Joly and Musset had come with empty hands, and it was soon evident that they proposed continuing the discussion and not undertaking an experiment, the result of which might compel them, in accordance with their agreement, to admit defeat. They suggested a whole series of preliminary researches, which had only a remote connection with the question in hand. They asked, for example, that a microscopic analysis of a litre of beer should be made; a frivolous and thoughtless proposal: to examine a litre of beer, drop by drop, under a microscope, would have taken some weeks, and could have thrown no light whatever on the question of whether samples of air taken in any locality would induce the development of living organisms. The committee, remembering the actual subject of the controversy, as accepted and limited by both sides, declared that they meant to keep to it; on which Pouchet, Joly and Musset backed out. It was an inglorious retreat. Pasteur saw his experiments succeed before the committee as in the laboratory; he retired victor in this long controversy, and the fact that his adversaries had run away was a confession of defeat. It was evident that Pouchet, Joly and Musset had no confidence in their cause, but if they had been more accomplished and accurate experimenters they might at least not have lost, even if they had not won. No one knew at that time that many germs, especially those found habitually in infusions of hay, are not killed by simple boiling. The capsule closed during ebullition no longer contains air. The germs, certain ones at any rate, deprived of oxygen no longer develop, but continue to live undetected, only showing their presence when, the point of the capsule being broken off, the oxygen which is essential to their growth and multiplication is again available.

Pasteur would probably have discovered these peculiarities when he first met with them, if his opponents had not run away. The three heterogenesists would have been able to show the committee capsules all invaded with organisms, and Pasteur would at first have been puzzled, but he would not have been long finding out what he discovered ten years later when an English doctor, Bastian, was ready to challenge the results of his experiments.

5. A Lecture at the Sorbonne.

These discussions on spontaneous generation interested not only the scientific world and certain Academies, they found their way into drawing-rooms and political newspapers. Here there was a hunt for weapons to combat philosophic and religious opinions which were not acceptable. The heterogenesists seemed to support the materialist doctrine; their adversaries, the panspermists (so called because they denied all new creations), were, whether they wished it nor not, on the side of the supporters of the Bible; nothing further was required to excite controversy.

Pasteur, however, was anxious to keep out of these squabbles. He thought, and was to say later on to the Academy of Medicine: "Science ought not to trouble about the result its work may have on philosophy. If, as a result of my experimental work, I happened to demonstrate that matter can become organized of itself into a cell or living being, I should announce it in these precincts with the legitimate pride of the discoverer, conscious of having made a wonderful find; and I should add, if provoked to do so: so much the worse for those whose doctrines and systems are not in accord with natural facts. It is with the same pride that I said what I did just now, defying my adversaries to contradict me: in the present state of knowledge the doctrine of spontaneous generation is a chimera; and I add in the same independent spirit: so much the worse for those whose philosophic and political ideas are confused by my investigations.

"Can it be said that in my inmost conscience and in the conduct of my life I should pay heed only to acquired science? I could not do it if I wished, for I should be taking away a part of myself.

"In each one of us there are two individuals, one the man of science who has thrown aside old notions, and who by observation, experiment and reasoning desires to obtain a knowledge of nature; the other the man of feeling, of tradition, faith or doubt; the man of sentiment who weeps at the death of his children, who cannot prove that he will see them again but believes and hopes that he will; who does not wish to die like a vibrion, and says that the force within him will be transformed. The two domains are distinct, and woe to him who wishes to make them encroach on one another in the imperfect state of human knowledge."

Everyone has not the beautiful serenity of the man of science. Heterogenesists and panspermists formed two camps, both sides being equally impassioned. The great amphitheatre of the Sorbonne could scarcely hold the crowd which thronged to hear Pasteur, when on April 7, 1864, he was invited to lecture on heterogenesis at one of the newly inaugurated evening scientific meetings.

He began in the rather solemn way to which he was inclined: "Many big problems are exciting attention at the present day and keeping all minds on the alert; the unity or diversity of the human race; whether man was created some thousand years ago or some thousand centuries; whether species are fixed or whether there is a slow and progressive transformation of one into another; is matter eternal and beyond it nothing; is the idea of God useless; these are some of the questions discussed among people to-day."

Pasteur gave a history of the problem of spontaneous generation and recalled that at the end of the eighteenth century a tremendous discovery, that of the microscope, had just revealed to mankind a new world, the world of the infinitely small. The doctrine of spontaneous generation, hardly disproved with regard to higher organisms, reappeared, saying boldly: "This is my domain."

Pasteur threw on the screen pictures of some of these microscopic organisms, the heterogenesis of which had been affirmed, such as the cellules of beer-yeast, spores of moulds, and infusoria; and he added, that the controversies which arose then, as they do to-day, among men of science were "the more violent and impassioned the more they were reflected by public opinion, which is, as you know, always divided into two great lines of thought, as old as the world itself, called in our day materialism and idealism. What a victory, Gentlemen, what a victory for materialism, if it could affirm that it was based on the proved fact that matter can of itself become organized, take life by itself, matter which has already in itself all the known forces! Ah yes, if we could only add that other force called life, life varying in its manifestations with the conditions of our experiments, what more natural than to deify matter? What good then to go back to a primordial creation before the mystery of which we can only kneel? What good the idea of God the Creator?"

Pasteur quoted a passage where Michelet affirms as a poet his belief in spontaneous generation. "Let us assist in the divine work, let us take a drop of water from the sea, and observe in it a renewal of the first creation. Will not this drop be the infusorium, the original monad, which vibrating and moving about, soon becomes a vibrion, and mounting higher and higher in the scale, to polyp, coral or pearl, will attain perhaps at the end of ten thousand years to the dignity of insect."

In the heart of this drop, which contains a little nitrogenous matter, marine mucus, or "fecund jelly" as Michelet calls it, his imagination pictures the spontaneous appearance of the first beings of creation, which by slow progressive transformations can, in the course of thousands of years, rise to the dignity of man.

Pasteur, however, was of opinion that on this subject there had been "enough of poetry of this sort, enough of imaginary explanations; it is time that science, the true method, reclaimed and exercised its rights.

"These matters have nothing to do with religion, philosophy, atheism, materialism or idealism. I might even add that as a scientist they concern me little. It is a question of fact. I have approached it without preconceived ideas, equally ready to admit the existence of spontaneous generation if experiment had demonstrated it, or to be convinced, as I now am, that those who affirm it have their eyes blindfolded."

Pasteur recalled the experiment by which Pouchet believed himself to have proved heterogenesis, and explained that this experiment was valueless, because it was performed over a mercury bath in which dust and germs abounded.

"There is no one among you, Gentlemen, who does not know that there is always dust suspended in the air. Dust is a domestic enemy that everyone knows. Which of you has not seen a ray of sunlight penetrating the crack of a shutter in a dimly-lit room. Which of you has not amused himself by following with his eye the erratic movements of those thousand tiny bodies, so small and so light that they are carried by the air like smoke. The air of a room is full of these specks of dust. Why does one not see them although they are well illuminated? We do not see them because they are so tiny, of such small bulk that the rays of light which each sends to our eye are lost, overwhelmed in the large number of rays which the smallest objects in the room send us, which are always large in comparison with these minute bodies. We do not see them by day for the same reason that we do not see the stars in the vault of heaven; but make it dark around us, make all obscure, and light only these tiny bodies, then we see them as in the evening we see the stars.

"We will darken this hall and throw a beam of light.

"You can see, Gentlemen, the dust dancing in the luminous ray. . . . If I had a little more time, I should say: look carefully at the ray of light, draw nearer to it, and you will see that the little specks of dust, though moving erratically, keep sinking lower and lower; fix your eye on certain ones and in a moment you will see that they are lower down, though still floating in the air. As they float they fall. It is thus that everything becomes covered with dust, our furniture and our clothes. Thus at the present moment dust is falling on all these objects, these books, these papers, this table, and on the mercury in this bath." And in dust are always germs.

After having shown how and why Pouchet was deceived—"it is easy to make experiments, but very difficult to make flawless ones"—Pasteur described his results, and in particular that of the magnificent experiment of the capsule with the long curved neck, open at the end, which after being boiled for a short time, kept a fluid very liable to alteration indefinitely unchanged. "This," said he, "is a most instructive experiment; for mark carefully that everything that is in the air, except the dust, can easily enter the vessel, and come in contact with the fluid. Anything you care to imagine in air—electricity, magnetism, ozone, even things still unknown, all can enter and come in contact with the infusion. There is only one thing which cannot enter—the dust suspended in the air, and this is the proof: if I shake the vessel smartly two or three times, in two or three days it becomes filled with animalculi and vegetable organisms. Why is this? Because air has entered rapidly and carried dust with it.

"After this, Gentlemen, I can say, in showing you this liquid: I have taken from the vast universe a drop of water and filled it with nutrient jelly, that is to say, in scientific language, filled it with elements required for the development of lower organisms. I wait, I watch, I question it, and ask it kindly to reproduce for me the first creation; that would be a beautiful spectacle! But it is mute! Mute during all the years since these experiments were commenced. Ah! It is because I have taken something away, taken from it in a moment the only thing which man is not gifted to produce. I have taken the germs which float in the air. I have taken from it life, for life is the germ, and the germ is life. Never again will the doctrine of spontaneous generation recover from the mortal blow dealt by this simple experiment." And he concluded: "No! Under no condition known to-day can we affirm that microscopic beings come into the world without germs, without parents of their own nature. Those who think so have been the sport of illusion, of ill-made experiments encumbered with errors which they have either been unable to perceive or unable to avoid." These words, delivered with profound conviction, were drowned in applause.

By saying "under no conditions known to-day," Pasteur, always having a regard for the exact truth, did not exclude the possibility of future discoveries. He was always ready to allow that in subjects of this kind "one cannot demonstrate a negative." But heterogenesists had claimed that they had proved experimentally that their doctrine expresses a reality, and Pasteur showed that this was not proved.

6. Dispute with Bastian.

The dispute which was to begin in 1876 with Bastian, showed how well justified was Pasteur's discretion and how error can creep into the most carefully carried out experiments.

Dr. Bastian was a distinguished English physicist, Professor of Anatomical Pathology at University College in London. He had studied the question of spontaneous generation on his own account, and upheld the doctrine of heterogenesis with fervent conviction. He said to

Pasteur: "If these organic liquids remain sterile in your hands, it is not at all because you have removed the influence of atmospheric germs from them, it is because you have not known how to discover physico-chemical forces capable of transforming the complex substances these liquids contain and of bringing about their organization into living bacteria. Take some urine, neutralized with a solution of boiled potash; protect them as securely as possible from the germs of the air, and put them into an incubator heated to 122° Fahrenheit (90° Centigrade). You thus introduce a physical influence, the temperature of 122° F., as well as the two chemical ones of potash and urine. At the end of from seven to twelve hours' exposure in the incubator, the fluid is turbid and swarming with microbes. How can you explain this development of microbes except by spontaneous generation? *My* experiment proves that, contrary to your assertions, the fermentation of urine is absolutely independent of germs from the air."

Pasteur repeated the experiment and obtained the same result. This by no means astonished him. He had already shown, in 1860, that in an alkaline medium germs are not destroyed at boiling-point, but this answer was not sufficient to convince Bastian, and a controversy ensued which was to last a whole year, and which was sometimes rather involved. Bastian was an ingenious investigator, and had a tenacious spirit; he multiplied objections, and so forced Pasteur to elucidate the minutest details of the question not previously studied with thoroughness. All our modern technique of sterilization was evolved from this.

Needham had already pointed out, during his first researches, that germs can already exist in a fermentable fluid and on the sides of the vessel containing it. All that was necessary was to close the vessels hermetically in order to protect them from the germs which float in the air. Those which stick to the sides of the vessel are less easy to destroy than had previously been believed. Pasteur knew that in a dry state many germs are highly resistant. To make sure of killing them a temperature of 180° C. must be maintained for half an hour. In practice Pasteur closed the vessels to be sterilized with plugs of wool and placed them in a gas oven; after half an hour's exposure at 180° C. the wool plugs were considerably singed, and the extent of their discoloration indicated that the necessary temperature had been reached. This method was called by the unsuitable name of *flambage*, or singeing.

There remained the sterilization of the liquid. In this case it was divided into two parts, that of the urine, and that of the solution of potash. Repeated experiments demonstrate that boiling at 100 C. is not sufficient to destroy the spores of certain bacteria in neutral or slightly alkaline or somewhat acid urine. The solution of potash is made with water and sticks of potash. The dissolved potash attacks the organic matter energetically and destroys it, it cannot therefore be the cause. Pasteur, however, studying with his collaborator, Joubert, waters from different sources, found that they all contain germs. Those waters only are sterile which have undergone a slow and thorough filtration through a great thickness of homogeneous soil. As these conditions are rarely present, it may be said that even the best spring water is not free from germs even when collected at its source, and germs are always contained in water taken from the tap of a supply pipe, and some always remain on the sides of vessels which have been washed.

Among these germs is usually the *bacillus subtilis*, which owes its name to its slenderness and is found everywhere owing to its great resistance to the ordinary means of destruction. This bacillus breaks up into spores, from which it again develops as if from an egg; and these spores, even more resistant than the bacillus, can withstand boiling for many hours. This treatment, however, which does not kill them, alters what may be called with good reason their *vegetative force*, meaning by this a variation in the facility with which they develop. After prolonged boiling these spores require oxygen in order to become again active. If one closes the capsule while the liquid is boiling, the air has been entirely expelled by the steam, the spores remain alive, but give no evidence of life. If one then breaks the point of the capsule, the indispensable oxygen returns, and the liquid is filled with microbes not brought by the air.

This is the secret of the experiments of Pouchet, Joly, and Musset. Hay-infusion almost always contains *subtilis*. This infusion boiled and regarded by the three heterogenesists, as well as by Pasteur, as sterile, was not so in reality. Pasteur would soon have discovered this if he had used it in his experiments; but his adversaries, uncertain of their technique, and unable to explain the variability of their results, did not dare to give battle.

This influence of oxygen is not the only one. Pasteur had previously noticed the importance of an acid or alkaline reaction of the liquid. On taking the question up again with his pupil Chamberland, he discovered once more that if the liquid is too acid the germs are not killed at a temperature of 100° C. but they no longer grow. If one reduces the acidity, and makes the fluid neutral or slightly alkaline, the germs regain their vitality and power of multiplication. This is what Bastian found with urine, which is normally acid. To destroy with certainty everything living in a liquid, it must be submitted for half an hour in an autoclave to a temperature of 120° C. It is necessary, in addition, that the receptacle containing the liquid shall have been exposed to dry heat. Heating a flask half full at 120° C. cannot destroy spores on the sides of a flask which are not wet.

Thus this controversy with Bastian had important results.

Heating at 120° in dry air ensures complete sterilization. These ideas were to introduce into surgery the most beneficent of revolutions.

CHAPTER IX

PASTEUR ELECTED TO THE ACADEMY OF SCIENCE

In 1861 the chemistry section of the Academy of Science had unanimously awarded to Pasteur the Jecker prize: "for a collection of researches most of which contributed to the progress of organic chemistry."

On the 8th of December, 1862, at his third attempt, Pasteur was nominated Member of the Academy, in the section of Mineralogy, by thirty-six votes out of sixty.

Before his election his claims had been discussed, and particularly, as they concerned mineralogy, his crystallographic work. Pasteur had discovered the relation existing between the crystalline structure and the rotatory power of the paratartrates. Right hemihedral crystals deviate polarized light to the right, left hemihedral crystals to the left. These words right and left apply to an observer looking at a crystal placed according to a clearly defined convention. Now it happens that the German convention is the exact inverse of the French. German crystallographers therefore said that right hemihedral paratartrates deviate polarized light to the left, and no one was surprised. It is quite obvious that the stump of a man's amputated right arm is seen either on the right or the left of the observer, according as it is observed from the front or behind. Some unscrupulous opponents, however, took advantage of this apparent contradiction to suggest that Pasteur's discovery was not one of an actual fact, and this might have succeeded in disturbing the minds of some of the electors. The surprise and indignation in the laboratory in the Rue d'Ulm were great. "When the news arrived," writes Duclaux, "the election was so near that there was not a moment to spare. I can tell you that we spent some pretty busy hours. There was to be a meeting that evening of the Philomatic Society where one might expect to find an audience of men of science. I was at once despatched to a carpenter's, and returned with saws, files, and a long squared block of pine. It was ten years since M. Pasteur had touched tartrates, but he still had their crystalline forms at his fingers' ends, and a few strokes of the saw, directed with wonderful precision, turned the pine block in a few minutes into crystalline forms with faces and facets. A few strokes of the file and plane to smooth the surfaces, a thin covering of paper to distinguish them and make them more easily seen, and there, all ready, were models of the crystals admirably adapted for use at the lecture on the subject which M. Pasteur planned to give that same evening at the Philomatic Society.

"The demonstration actually began as a lecture but ended as a philippic, when towards the close, and after having pointed out the incredible misunderstanding out of which capital had been made, M. Pasteur put his adversaries into the dilemma of having to confess either ignorance or bad faith. He ended by giving them this choice of alternatives, saying, if not in so many words: 'If you understood the question, what happened to your consciences? and if you did not understand it, why did you interfere?' M. Pasteur has achieved many triumphs in discussion since then, but I do not think that any were better deserved than the one he obtained by this pointed and convincing improvisation. He was still bubbling over with it as we went home together on foot, and I remember making him laugh by asking why, when he had fairly let himself go, he had not ended by hurling his wooden crystals at the heads of his adversaries."

This instinct for a fight against dishonest and clumsy opposition is one of the characteristics of Pasteur's scientific temperament; he often had occasion to display it. Duclaux has said of his chief: "When people brought against him only unsound argument, mere phrases, or ill-made experiments, he set about buffeting his adversary with a violence that the spectators, and especially the person concerned, found excessive. He had, however, no real rancour against individuals, he was only incensed against false ideas, and this hatred was but the reverse side of his profound love of truth.

CHAPTER X

VINEGAR

PASTEUR'S studies on fermentations and spontaneous generation had led him quite naturally to interest himself in the changes in alcoholic liquids which lead to the formation of vinegar.

When wine is left in an uncorked bottle it goes sour, and a thin film often forms on the surface. The wine growers of the south have long noticed this in wine left in open barrels, and use it in making vinegar for their own consumption. Into a barrel kept for the purpose and containing vinegar covered on the surface with this scum, which they call *mother of vinegar*, they pour the dregs left at the bottom of barrels and bottles ; experience has taught them that the *mother* ought not to be submerged, for when this happens the *vinegar maker* no longer works. The Orleans manufacturers make vinegar by this process on a big scale.

In Germany the process is different. The ends are knocked out of a number of barrels ; these are arranged in a column, one above the other, and filled with beechwood shavings, care being taken not to press these down, so that air is in contact with them and can circulate freely. A weak alcoholic solution, to which a small quantity of acetic acid and sour beer or wine, or other decomposing matter, has been added, is sprayed on to the top of the column. The fluid flows over the shavings, ferments, and gets warm, so that a current of air is set up in the column, resembling the draught in a chimney, with the result that the liquid flowing in thin layers, and constantly bathed in fresh oxygen, is rapidly oxydized and converted into acetic acid.

Doebereiner had discovered that if one pours a little alcohol on powdered platinum, that is platinum-black, the alcohol is transformed more and more completely by oxydation, first into aldehyde, then into carbonic acid. These changes are shown chemically by the following formulæ:

(1) C_2H_6O (alcohol) $+ O = C_2H_4O$ (aldehyde) $+ H_2O$
(2) $C_2H_4O + O = C_2H_4O_2$ (acetic acid) $+ 2H_2O$
(3) $C_2H_4O_2 + O_4 = 2CO_2$ (carbonic acid) $+ 2H_2O$

or

(1) $C_2H_6O + O = C_2H_4O + H_2O$
(2) $C_2H_6O + O_2 = C_2H_4O_2 + H_2O$
(3) $C_2H_6O + O_6 = 2CO_2 + 3H_2O$

The platinum undergoes no alteration and seems to act simply by its presence. It is in fact the oxygen condensed in the pores of this fine metallic dust which acts on the alcohol and consumes it. To Liebig the action of beech-wood shavings was in every way comparable to that of platinum-black. These also act only by their presence, and the proof is that after years of manufacture the shavings look as new as on the first day.

This explanation did not satisfy Pasteur. In the German method the oxydation of the alcohol is very rapid. Besides in the course of his investigations on spontaneous generation, he had found by numerous analyses of the air in his capsules, that rapid oxydation of organic matter in contact with air, only takes place in the presence and by the action of organisms. This oxydation is very slow when germs have no part in it; and actually it is quite easy to prove that *mother* of vinegar consists of innumerable organisms which spread like a veil over the surface of the fluid—hence the name *mycoderm of vinegar*—and which multiply very rapidly. The cellules, twice as long as they are broad, constricted in the middle, and always arranged in chains, do not exceed a thousandth of a millimetre in breadth; they have enormous power of producing fermentation. Duclaux has calculated that "three hundred thousand millions of cellules weigh about a gramme and turn into acid, in four or five days under favourable conditions, ten kilogrammes of alcohol. That is to say that each of these cellules requires two thousand times its own weight of the substance it feeds on per day. The oxydation of these ten kilogrammes needs the participation of more than six kilogrammes of oxygen, that is more than there is in fifteen cubic metres of air." This explains why the mycodermic *veil* requires so much air: wine does not turn sour in a corked bottle.

When for some reason or other the mycoderm grows feebly, its oxydizing action stops at the first stage, and the alcohol is converted into aldehyde, easily recognizable by its penetrating odour. At other times if the alcohol fails, the mycoderm can feed on the acetic acid already formed, and by further oxydation converts it into carbonic acid: "that is to say," as Duclaux writes, "when starved it consents to accept food which had hitherto collected in the surrounding fluid,"

$$C_2H_4O_2 + O_4 = 2CO_2 + 2H_2O$$

Pasteur, always ready to apply his discoveries to human physiology, compared the oxydizing action of the mycoderm to that of the corpuscles of the blood, whose function it is to carry oxygen to the tissues. What would happen if the blood corpuscle, unequal to its task, could not carry oxydation far enough, like a mycoderm which stopped short at the aldehyde stage? This was a valuable hint to pathology.

From such a complete study of the life and, if one may say so, of the habits of the mycoderm, Pasteur devised a rational method of making vinegar. Sow some cellules all over the surface of the mixture of wine and vinegar which is destined to form acid; it is found covered with a thin film in twenty-four hours; soon this film thickens and wrinkles, so rapid is the multiplication of the cellules, which are closely packed and crowded together. In this way the manufacturers can at will rejuvenate and renew the *mother*. They are no longer at the mercy of *veils* so thin and delicate that a sudden quick change of temperature may ruin their activity. The veil may break, sink and be drowned, and this, before Pasteur had shown how it could be renewed, was a serious matter, as a new one was difficult and costly to obtain.

Pasteur had made known the result of his studies in two communications to the Academy of Science in 1862, and also in a *Note on Acetic Fermentation* published 1864 in the Scientific Annals of the École Normale Supérieure. Some vinegar manufacturers applied his method successfully, others less skilful made unsuccessful attempts. In 1867 the Mayor and the President of the Chamber of Commerce at Orleans begged Pasteur to come and teach his method to the manufacturers of their town. This lesson was admirably clear.

Pasteur wanted to show his audience, to begin with, the difference between wine and vinegar. He produced two exactly similar distilling apparatuses: the first containing wine, the second vinegar made from wine of the same kind. He heated them and obtained by distillation two liquids equally clear and colourless. He boiled the liquid obtained from the wine, and the vapour given off burnt when a candle flame was applied to it; no such result was obtained from the second liquid.

"The ancient chemists called all volatile material obtained by distillation *spirit*; it was the quintessence of the substance. *Spirit of wine*, which they called also *ardent spirit* because the vapours were inflammable in contact with air and a burning body, is called alcohol when it is freed by distillation from all the water with which it is necessarily mixed. The name of *acetic acid* was given to the spirit of vinegar when freed from water."

Pasteur proved, by a simple and convincing experiment, that vinegar is produced by the combination of the oxygen of the air with the alcohol of wine. He placed in a large glass flask, wine prepared for acidification, the wine occupying only a small part of the flask, so that above it was a large volume of air. Pasteur corked the flask carefully, turned it upside down and plunged the neck into a water bath. When the transformation of the wine into vinegar was completed, he uncorked the flask: the water from the bath ascended into the flask as though a partial vacuum existed there, and it can be shown that that quantity of water which entered the flask corresponds to a fifth of the volume of air before the experiment,—that is the proportion in which oxygen exists in air. The oxygen has actually disappeared, the gas remaining in the flask is nitrogen, and presents all its characteristics, a lighted match when introduced going out as if thrown into water. Thus it was clearly demonstrated that the conversion of wine into vinegar is a phenomenon of oxydation.

The transformation is performed through the intervention of the *mycoderma aceti.* That is to say it never occurs in its absence, but its presence is not a complete proof; it may be—and this opinion was held by many scientists—a mere coincidence. This mycoderm is not the only thing present in the manufacturer's vats; there are found also innumerable small animals known by the name of *anguilles de vinaigre,* vinegar eels; why should these not play a part in acidification?

Here comes in the experimental method, "a method so certain when rigorously applied, to which modern science owes its tremendous progress. The danger always lies in a faulty interpretation of the facts. The most skilful stumble at every step. The great art consists in devising decisive experiments, leaving nothing to the observer's imagination. At the beginning of an experimental research on any fixed subject, wings must be given to the imagination. At the moment for drawing conclusions and interpreting collected observations, the imagination must, on the contrary, be made to give way and submit to the actual results of the experiments."

Duclaux has clearly explained the words which thus clearly describe Pasteur's method of working and give in part the key to his genius: "In experimental science the imagination applied to the study of concrete facts, commences with an act of faith, or of doubt, which is fundamentally the same thing. Sometimes without any attempt at criticism every corner of the science seemed plunged in obscurity, or else bathed in unexpected light. Certain accepted truths seem suddenly doubtful; others unrecognized make confusing protests. The mind is in a whirl. By replacing things which appear uncertain by those which it accepts as true, it takes a new and usually more simple view of the subject, and one with which it satisfies for the time being that desire for light which exists in the depths of the human soul.

"Having once created this mental picture, its rôle is ended. It must retire immediately from the stage on which it would shed misleading lights. The laboratory takes up its part. The scientist must submit the bright light which has flashed across his brain, a light which has sometimes dazzled him, to experiment, as if he had no confidence in it. He must treat it as an enemy. I cannot deny that this path is difficult. Many do not succeed in following it but remain gazing at the mirage, either because their imagination is too strong, or because of a defective training in experimental work."

This act of faith was, in crystallography, the belief in a relationship hitherto undemonstrated between crystalline form and rotatory power. In the case of fermentations it was the belief that they depended upon the life of yeasts.

A mixture of pure alcohol and water never develops acid. Before the development can take place, albuminous matter, such as exists in wine, must be added. The old theory stated that this dead albuminous matter decomposes and acts as a ferment.

Pasteur replied with an experiment. He introduced into a glass phial which was afterwards hermetically sealed, wine and air, but he took the precaution of heating them both first. Under these conditions wine is never converted into vinegar. Can it be said that the albuminous matter has been affected by the heating? Pasteur opened the phial and allowed ordinary air free access to the heated wine. This is all that is necessary to produce the development of acid. The *mycoderma aceti* is one of those small growths, called *spontaneous*, which form on the surface of fluids suited to their development. In wine, in vinegar, suspended in the air, everywhere, exist the germs of this little plant.

"Do you wish to produce some mycoderm for the first time, all that is necessary is to put a mixture of wine and vinegar in a warm place. After some days you can see small greyish spots appearing here and there, diffusing light instead of reflecting it as does the surrounding liquid. These spots will extend progressively and rapidly. This is the *mycoderma aceti*, born *spontaneously* by means of the seed contained in the wine or in the vinegar, or else deposited by the air, just as one sees fields clothe themselves with various plants springing from seeds existing naturally in the soil or carried by the wind or by animals. The comparison holds true even with regard to the last mentioned agents, for if you place wine in a warm spot, it is remarkable how often one shortly sees appear the small reddish flies which frequent vinegar factories or any place where vegetable matter is going sour. They too, with their little feet and their probosces, can bring seed from an adjacent factory."

The albuminous water does not act as ferment but as food to the ferment. Pasteur gives conclusive proof of this by showing that one can do without this material and still obtain acid from a mixture of pure water and alcohol. Add to this mixture some crystalline salts, alkaline or earthy phosphates, and phosphate of ammonia ; it is not its favourite mixture, and the mycoderm does not develop vigorously in this medium, but it develops sufficiently well to perform its function and oxydize the alcohol.

The *eels* of vinegar are microscopic beings which multiply with extraordinary rapidity. They too are found in all the vinegar vats of Orleans. Far from assisting in the manufacture as was long believed, they are extremely harmful. The reason for this is easy to understand. Like the mycoderm, they require oxygen for their development, and there ensues between the two a fight, in which the mycoderm does not always win, for this gas which is essential to their life. When the mycoderm does not succeed in getting rid of its adversary and spreading itself over the surface, acidification is arrested.

Care must be taken not to allow the action of the mycoderm to continue after all the alcohol has been converted into acetic acid, because the acetic acid may in turn be oxydized and converted into carbonic acid. The ethers and aromatic elements which give the vinegar its bouquet would undergo a similar alteration. Thus putrefaction may take possession of the neutral and insipid liquid which is no longer protected by the old acidity.

In the German method nothing comparable to the *veil* of the French vats is found, but if one scrapes the surface of one of the beech-shavings, which appear to keep their original freshness, one can easily recognize, under the microscope, mycoderm cellules. At Orleans vinegar is made from wine in which the cellules find the abundant nourishment which allows of rapid multiplication. In Germany they are supplied with a solution of alcohol to which has been added a little sour beer, which is a scanty diet. The mycoderm puts up with it, but develops so little that its existence was long doubted. It is this, none the less, which causes the acidification.

Liebig was far from pleased when he read this work of an adversary with whom he had already met and fought. He was at this time one of the leading chemists, full of years and honour. For more than thirty years he had taught a theory of fermentation which had been universally approved; and here was a man, young from his point of view, who set himself up to prove an action, so long believed chemical, to be a vital one, and in a case too where beech-shavings played a part so exactly comparable to that of platinum-black in the oxydation of alcohol.

Liebig wrote two memoranda to defend his ideas. It was no doubt true that the nutrition of the cellule is on final analysis resolved into a chemical reaction, but it was a great mistake not to be willing to recognize the specific nature of fermentations and their close correlation with the activity of living organisms. Liebig denied that the *mycoderma aceti* played any part in the German method of making vinegar, and the proof of this, he said, is that a wood shaving which has been used for twenty-five years in a large Munich factory, showed no trace of mycoderm, even under the microscope.

Pasteur was not long in refuting the lengthy dissertations of Liebig. He invited him to submit their differences to the judgment of a committee of the Academy of Science, and undertook to show mycoderms on every shaving which should be brought to the committee. He offered to convince him by another method. Let one of the Munich manufacturers fill one of his barrels with boiling water, and keep it so for half an hour; the mycoderm would be destroyed, and the barrel be useless to the manufacturers for a long time, until in fact a fresh mycoderm had been able to enter and reproduce itself there, although according to Liebig's theory the boiled barrel ought to function just as it did before.

Liebig did not reply.

CHAPTER XI

DISEASES OF WINE

The acidification of wine is a disease, and assuredly that to which it is most subject. Pasteur having now discovered the responsible cause, was able to indicate the means of destroying or avoiding it. There were, however, many other diseases which were the despair of the wine-growers, some peculiar to certain brands: claret suffered from *tourne*; burgundy from *amer* or bitterness; champagne from *graisse*, a sort of viscous ropiness. Was not a microbe responsible for each of these, as well as for *acide*? Pasteur put this question to the Academy of Science in the month of January, 1864. He had already found the answer to it.

"I have," he said, "reached this conclusion: that the changes which take place in wine are due to the presence and multiplication of specific microscopic vegetations."

He spent the vacations of 1864 in studying this question. He had installed an emergency laboratory in a disused Café on the outskirts of Arbois. Clumsy apparatus, manufactured by the local tinker and blacksmith, served to take samples of wine in the cellars belonging to friends of his childhood, and a good deal of fun was made of him as he passed through the streets with this quaint outfit; but the interest of his investigations was soon apparent.

His pupil Duclaux writes: "Every time that the wine-tasters let him know that any peculiar defect in flavour had been observed, he found, mixed with the yeast at the bottom of the cask, some distinct species of microbe, so that he was soon able to make the inverse test, that is to say to indicate in advance the flavour of the wine by examining its deposit. Sound wines contained only yeast."

Thus Pasteur had completely solved the problem. He expounded the whole question two years later in his *Studies in Wine.*

He had not contented himself with studying the diseases which attack wine at various ages; he wished also to understand the causes of the constant change which wine undergoes, and the reason of its maturing. Wine-growers are possessed with the idea that air is the great enemy, and the reason for this is no doubt that wine exposed to the air goes sour very quickly. A great point is made of avoiding any aeration of the wine during racking; sulphurated wicks are burnt in the barrels before they are filled in order to expel the air from them, and to prevent its re-entry the barrels are constantly filled up. Finally, as wood is not impervious to air, it is considered that wine keeps less well in casks than in bottles. Whatever precautions may be taken it is impossible entirely to prevent contact with air, and wine, like water, must contain liquid air. Now Boussingault had found that wine in barrels only contained nitrogen and carbonic acid, the oxygen had been absorbed; and Bertelot demonstrated that it was an excessive absorption of oxygen to which must be attributed the change in wine known as *flatness.*

Pasteur could not understand wine being unable to bear oxygen, but he asked himself whether this gas might not be necessary to the growth of the microbes which are always ready to invade the wine, and if in consequence the precautions taken to prevent the approach of air had not been in reality prophylactics against the development of disease.

Everybody knows the *mycoderma vini* or *fleurs de vin,* the little white pellicules which form on the surface of the liquid in bottles or in casks. It is a fungus which is known to be much less dangerous than that of vinegar, which it resembles in absorbing the oxygen of air, but from which it differs in that it produces complete oxydation; it immediately transforms alcohol into carbonic acid gas and water without passing through the dangerous intermediate form of acetic acid. Carbonic acid, being heavier than air, spreads itself over the surface of the liquid like a layer of oil on a surface of water, and thus constitutes an effective protection against a fresh supply of oxygen.

Having arrived at this point in his study, Pasteur soon recognized that it is only the parasites of wine which are its enemies, and that, contrary to the hitherto received opinion, it is the slow and progressive action of the oxygen which develops in the wine as it matures those qualities latent in the new wine. New wine is thick and highly coloured, it has a sharp harsh flavour, it is *green* or *rough* ; little by little it undergoes alteration, it loses its colour, it becomes clearer, it acquires a mellower and finer flavour, and reaches, at an age which varies in different brands, its highest point of excellence. From this moment the oxygen, continuing its action, spoils the wine, causes it to deteriorate gradually, and ends by transforming it into a flat insipid liquid which retains none of its former value.

Pasteur has demonstrated that it is sufficient to protect wine entirely from the action of oxygen to prevent its maturing. He takes wine from the vat at the moment when, fermentation having ceased, the wine is saturated with carbonic acid ; he fills a bottle up to the top of the neck, managing to avoid all contact with the air. In the bottle, hermetically sealed, this wine remains indefinitely *new wine.*

The phenomenon of *flatness* is due to a too rapid absorption of oxygen. The *flat* quality often disappears of itself when the dissolved oxygen is restored by means of oxygenation.

Since the diseases of wines are caused by parasites, they may be prevented or checked by destroying these parasites ; but it must not be forgotten that the flavour of wine is a very delicate thing ; one knows how it is affected by heat: hot wine is no longer wine. Nevertheless it was to heat that Pasteur had recourse after several unsuccessful efforts made with antiseptics which had to be innocuous to the consumer and proved in this necessarily high dilution equally innocuous to the microbe.

Pasteur had learnt from his studies in spontaneous generation that in an acid medium like wine microbes are particularly sensitive to heat, and that one can prevent their multiplication without raising the temperature to a degree which would kill them. On the other hand it was probable that wines recently aerated by drawing off and decanting were more delicate than wines which have been long undisturbed and which contain no free oxygen, and that therefore it would be better to treat only the latter.

It was by drawing inspiration from these purely personal ideas that Pasteur made his experiments. He soon recognized that a heat of 55° C., kept up for several minutes and protected from air, was enough to obtain the desired result. He had just discovered the method of preserving *alterable* liquids, such as vinegar, beer, and milk, which has appropriately received the name of pasteurization.

Numerous trials have proved that wines heated by Pasteur's process can, without losing any of their qualities, bear long journeys and voyages in the course of which wines of the same brand, which have not been heated, undergo alteration.

CHAPTER XII

DISEASES OF SILK-WORMS

1. Before the Time of Pasteur.

Duclaux has related that one day in the spring of 1865 Pasteur, on arriving at the laboratory, said to him with some emotion: "Do you know what M. Dumas has just asked me to do? To go to the south to study silk-worm disease."

Pasteur was greatly embarrassed. He had never touched a silk-worm. On the other hand, Dumas was one of the masters whom he most esteemed, and who had shown him the most kindness. It would be necessary to give very grave reasons for refusing his request, especially as it had been made in a semi-official manner. Dumas, a Senator from Gard, had been asked to prepare a report on a petition signed by 3,754 proprietors in the silk-producing districts, asking for official assistance in fighting an epidemic which was ruining them.

At the beginning of the Second Empire, the sale of cocoons had brought in a revenue of nearly a hundred million francs. If one bears in mind that this harvest was obtained in six weeks—six weeks of hard work, it is true—one can imagine what a valuable addition this was to the resources of the southern farmers.

Pasteur had only the vaguest idea of sericulture. He hastily ran through the books recently published on the subject, and thus acquired a certain amount of knowledge of the habits of the silk-worm. At the moment when the first leaves of the mulberry begin to unfold, the eggs, or *graines* as they are technically called owing to their resemblance to certain vegetable seeds, are hatched by exposing them to a gentle heat. When the grubs appear they are covered with young leaves, on which they immediately begin to feed; they are placed with the leaves on trays made of reeds, and known as *cannises*, because the reed used is the cane of Provence. On these trays they spread themselves out as they develop. Four times they change their skins, and while this *moult* is taking place they appear to sleep. After the fourth change they display immense voracity; their mandibles as they attack the leaves making a continuous noise, which Pasteur compared to the beating of rain on trees during a storm. On this diet they grow very fast, and rapidly attain their maximum size. Soon they cease to eat; they raise their heads and seem uneasy; at this moment the breeder places rows of twigs between the reeds, and the worms creep up them in order to spin the cocoons which are to protect them during the change into the chrysalis and into the moth. A fortnight or three weeks after climbing the twigs they are fully developed; the moths pierce the cocoons, emerge from their prison of silk, mate, and lay their eggs.

Thus from egg to egg, from seed to seed, the evolution of the silk-worm does not take more than sixty days, thirty-five of which are occupied by the period from the hatching of the egg to the completion of the cocoon.

The pierced cocoon is useless for silk, therefore when eggs are not required, the chrysalids are suffocated by being placed in a steam oven.

In the country of the mulberry, to which is gladly applied the name of the Golden Tree, in gratitude for the riches which it produces, the silk-worm breeders call themselves simply *magnaniers*, the silk-worm is the *magnan*, the nurseries *magnaneries*, and the pretty name of *magnanarelles* is given to the women who pick the leaves and look after the worms.

The production of eggs soon became specialized. When a culture had been remarkable for the regular development of the worms and the beauty of the cocoons, it was devoted to the production of eggs. The eggs, weighed by *ounces*, were, on account of their love of air, kept in cardboard boxes perforated with numerous holes. Things continued thus for many years, the breeders making a point of improving their eggs, and the farmers being, except in cases of accident, fairly certain of their harvest and profits.

However, during the previous twenty years *accidents* had become more and more frequent. Hatches were irregular, worms developed slowly and badly, many died before the fourth moult, and those which survived it had difficulty in spinning their cocoons. Evidently the seed was bad. It was changed, eggs being imported from distant countries, from Turkey, and even from Japan. After a few good harvests the failures began again—the disease had spread right round the world. This disease seemed to be epidemic and contagious, judging from the fact of its spreading so universally, and from its suddenly appearing in a culture which had started perfectly well. Troublesome facts were cited; a mixture of two sorts of eggs, one from white and the other from yellow cocoons, raised in the same *magnanerie*, gave bad results in the one case, and excellent ones in the other; was it therefore possible to believe in its epidemic and contagious character?

In his report to the Senate, Dumas pointed out the obscurity of the whole question: "Eggs, worms, chrysalids, moths, all are affected by the disease. Whence does it come? Nobody knows. How is it communicated? That is also unknown, but the attack is recognizable by the appearance of brown or blackish spots." Owing to the fact that these little spots resembled grains of black pepper, de Quatrefages gave to the disease the name of *pébrine*. All those marked with these spots were not, however, diseased, and those not marked sometimes produced bad seed.

Several observers had noticed, when examining the affected worms and moths under the microscope, that they contained many parasites, which, for lack of a better name, were called *corpuscles*; but other scientists affirmed that these corpuscles were an unimportant organism existing in all moths. Dr. Osimo, of Padua, having observed corpuscles in the eggs, had advised the rejection of all eggs laid by moths having an excessive number of corpuscles, but he did not seem to attach much importance to this suggestion, and did not quote a confirmatory experiment. Another Italian scientist, Professor Cantoni, found corpuscles in worms derived from immune moths, from which he concluded that the examination of moths under the microscope was unfortunately as useless a means of prevention as all those hitherto recommended.

All this history was fairly discouraging, but Pasteur knew nothing of it when Dumas asked him to come to the aid of his fellow-countrymen. When he sought to excuse himself on the ground of incompetence, Dumas said: "So much the better, you will have no ideas but those which are the result of your own observations," a theory which, as Duclaux points out, may not always be paradoxical, but which could not safely be propounded to everyone.

Pasteur accepted the mission offered to him, for he realized that the object of it was perhaps not alien to his present studies; he had long believed that his researches in fermentation and in spontaneous generation would not be without application to animal physiology and pathology. He left for Alais on June 6, 1865.

2. First Observations and First Method of Egg Production.

Pasteur's researches were to last six years. Nothing could be more interesting than to watch a man of such fine intelligence attacking a question which was so complicated and so obscured by prejudice and badly made observations; to see him hesitating, making mistakes, and straying from the right path, but always knowing how to find the way back to it, thanks to his entire dependence on experiment and the teaching of facts.

It is a great trial, said his pupil and collaborator Duclaux, to work always under the public eye, and in an official position, constantly facing a menace with which one has to cope, but it has its advantages: "He had no right to preserve, with regard to this branch of his researches, that Olympian silence which he liked to maintain up to the day when he considered his work ripe for publication. As a rule he did not say a word about it, even in the laboratory, and his assistants saw only the outside and skeleton of his experiments, and nothing of the object with which they were carried out. Here, on the contrary, he was obliged to speak as soon as he had discovered anything, to challenge the judgment of the general public and of the industry on all that he found out in his laboratory. Thus it is that we are able to follow the working of his inmost thoughts."

Pasteur wished first of all to procure from the breeders of Alais all the useful information which they had been able to obtain with regard to silk-worm disease. There was a fine hubbub! Each one had his own theory: it was a plague, a form of cholera, it was miasmic or mephitic. All sorts of remedies were advocated, and the most fantastic were not the least popular. Pasteur did not dwell on them, but set to work to verify the suggestions of de Quatrefage. He easily found the corpuscles in the diseased worms and moths, and recognized the pebrine spots on the skin of the worms. An instinct persuaded him that these microscopic corpuscles, on which opinion was so much divided, must be either the symptoms or the causes of the disease.

Quite at the outset of his researches he made, in one of the *magnaneries* which he visited, a troublesome observation which might well have set him off on a wrong track. The proprietor had two *chambrées*, both hatched from Japanese eggs; one was doing very well, the other badly; the first was going to yield a splendid harvest, the second was producing only just a few isolated cocoons. Pasteur saw, to his great surprise, that the chrysalids and moths of the first lot nearly all contained a great many corpuscles, whereas it was quite difficult to find any in the other. He continued to observe those of the second chamber, which completed their evolution, and found that the number of corpuscles increased with the age of the worm, that this increase continued in the chrysalids, so that the corpuscles were in great abundance in the moths.

How were such facts to be interpreted? Pasteur, who believed, like everybody else, that there was only *one* disease, considered himself obliged to interpret the result of his first observations thus: the same disease had attacked both chambers, but in the case of the first in a milder form and at a later date, so that the worms about to climb the twigs had still strength to spin their cocoons; the second had been attacked earlier, and with more virulence, so that the worms were exhausted before the fourth moult. The corpuscles are produced by the disease, and appear earlier or later in different cases.

This explanation was faulty, and Pasteur waited to correct it by experiment, but from the accurate fact that the corpuscles are a sign of the disease it follows that non-corpusculous moths should be selected for the production of eggs.

As soon as the 26th of June, a fortnight after his arrival, Pasteur set forth before the Agricultural Committee of Alais an almost infallible method of doing this. Each pair of moths should be isolated in a separate cell at the moment of egg-laying. The female would there lay her eggs, and then both she and the male would be dissected in order to search for corpuscles. If none were found the seed could be considered sound.

This was, on the whole, the same as Osimo's method, which, when tried by Cantoni, had given only bad results.

Duclaux has, with his usual perspicacity, shown how Pasteur, on seeing the corpuscles, immediately grasped the capital importance of their presence and of their action:

"The point is that, differing from his predecessors, he went into the question not with vague hypotheses or obscure ideas, but with an exact belief, the elements of which had been obtained from his previous studies. To him, after his researches on ferments and on the diseases of wines, the entrance and development of a microscopic being in a living animal must show itself by visible changes, which could only be disorders and would constitute a disease. To prove the accuracy of this idea, of this inductive interpretation of phenomena, there was only one apparently quite simple thing to do, namely, to procure healthy eggs, preserve the grubs from contagion during development, and then see whether or no they succumbed to the prevailing malady.

"The idea was so simple that already it was no longer new. The suggested experiment had been made and had not succeeded. It ought, however, to succeed, and has succeeded thousands of times since. How is the original failure to be explained? It is here that we shall find again, even in the performance of the experiment, and along with his practical dexterity, the influence of Pasteur's original belief and of his governing idea. Up till the time of Pasteur the aforementioned experiment, that of the protection from contagion of the eggs of non-corpusculous moths, had been performed in a careless manner, almost in the dark, because it did not agree with a hypothesis, with a possible case, judged *a priori* to be no more probable than any other; sound eggs might produce sound worms, but it was just as likely that they would produce diseased worms. If when starting on a journey by night one were to carry a lantern giving such an uncertain light, and if, in addition to this, one were unacquainted with the difficulties and windings of the road, one would be sure to go astray, and this is what happened to M. Cantoni. Pasteur, on the contrary, had a bright inner light; the world of the infinitesimal was familiar to him; he knew how to avoid the pitfalls on the road, and in this case he distinguished himself by drawing a new and fertile conclusion from an old idea by the way he treated it in his experiments."

3. AT PONT-GISQUET. COMPARISON OF RESULTS IN BREEDING FROM SOUND AND FROM DISEASED EGGS.

In 1866, Pasteur, having been entrusted by the Minister of Agriculture with a new mission, established himself on the estate of Pont-Gisquet, near Alais, with his pupils Gernez and Maillot.

Duclaux has given a charming description of the estate and the establishment:

"Shade, water, an orangery, which made an excellent laboratory, *magnaneries* for practical experiments, mulberry-trees on the grounds, a spacious house, clean and comfortable, where all lived together, all this no doubt contributed to the success of the investigations, and to the energy and good health of the workers and their chief. But the conquest of this Eden was not accomplished without difficulty.

"At first the mission had been obliged to content itself with a hotel for board and lodging, and, for the experiments, with a rough and ready laboratory arranged at the house of a silk-worm breeder near the town. The food was bad, one slept little and worked with difficulty, and this state of things lasted until one day Friend Gernez took advantage of Sunday's leisure to explore the neighbourhood of Alais in the hope of finding more comfortable quarters. The providence that watches over men of science, or rather over silk-worms, led him to Pont-Gisquet, which, as seen through the gate, appeared to be a paradise. But this paradise seemed not to be to let, and the gate did not open in spite of repeated shouts and pulls at the bell. The reason was that the proprietor was away, and everything left in charge of a gardener fond of peace and quiet, whose reception of Gernez, when at last he succeeded in climbing over a wall, was more than cold. *Violenti rapiunt illud!* Gernez was clever enough to gain the consent of the gardener, and then that of the owner, so that within a week the move was made to Pont-Gisquet.

"M. Pasteur has himself, at the end of his *Studies on Silkworm Disease*, been careful to recall the happy days which he spent there; he has also been kind enough to thank the assistants who accompanied and helped him for their devotion and their zeal. Being myself the one who spent least time there, I can speak of what the others, Raulin, Maillot, and especially Gernez, did. I do not believe that a more united or harder working community was ever grouped round a chief. It is hardly necessary to say that we did not do the thinking part of the business, for M. Pasteur was still at that time a secret worker, who kept all his plans and ideas to himself, but one could guess them, or one could imagine that one guessed them, and that gave a piquancy and interest to the thousands of experiments which occupied our days. And the experiments! and the superintendence of trial cultures! And all the worry over the constant fear of the invasion of mice, which preferred silk-worms to the most succulent bait! And the feverish gathering of mulberry-leaves when rain seemed imminent! Everybody turned to: Mme. Pasteur, her children, the assistants, *magnanarelles*, everybody, even the crabbed gardener, who, in spite of himself, had not been long before starting to work with us for his country."

Gernez, on his side, wrote of this season of 1866: "It was a period of intense work. Pasteur undertook a great number of trials, which he followed himself down to the minutest detail; he only admitted our help in similar operations which served to check his own. The consequence was that in addition to the fatigues of the day, which our youth enabled us to support, he had all the anxiety attendant upon the experiments, the disagreeable surprises of a correspondence abounding in criticism, and the necessity of answering the importunate. On the other hand, in order to clear the ground, it was necessary to disentangle from the mass of evidence produced in France and abroad, what would be likely to have any value. Finally there were all the remedies, each supposed to be infallible, which were suggested for the cure of the disease; each had to be examined with the minutest care before arriving at a decision as to its efficacy. At the same time a vast number of experiments were being made, and applications were coming in from all sides for advice on the most varied and unexpected points."

In order to look for the corpuscles, a little piece of the abdomen of the moth was removed with the forceps, and the inner side of the fragment examined under the microscope. This procedure was inspired by Pasteur's idea that *the disease* of silk-worms was a constitutional malady, affecting the whole organism, and that the corpuscles, formed at the expense of cellular tissue, must be found everywhere. Unfortunately this hypothesis was false; the corpuscles, which were the cause and not the effect of the disease, only existed in certain parts; in order to be practically sure of finding them it was necessary to examine a particle formed of elements representing the whole moth; this was done later by placing under the microscope a drop of the pulp obtained by braying the moth with a little water in a mortar.

But although Pasteur, who was observing extremely complicated facts quite at the beginning of his investigations, had been led to incorrect conclusions, nevertheless he had derived from them a singularly fertile resolution, which was to follow and compare the results of breeding from healthy eggs and diseased eggs. This is what he did during the season of 1866, and he thus determined the effect upon the breed of eggs obtained from more or less corpusculous moths.

He saw first that, as he had predicted, the harvest was bad in proportion to the amount of corpuscles contained in the moths which produced the eggs.

There was another interesting point: corpusculous moths could produce eggs which resulted in fairly good harvests; but all the moths from these eggs contained a very large number of corpuscles, and the next culture gave bad results. This explained a fact which had often been observed, namely, that eggs obtained from a successful hatch often gave only a poor harvest or a complete failure. This proved that the beauty of the productive worms and moths is no guarantee as to the quality of the eggs.

A third rather surprising point is this: even in the worst chambers one finds moths obtained from corpusculous parents which nevertheless contain no corpuscles, and are capable of producing good seed. This fact is of great importance, since it makes it possible, by careful examination, to obtain healthy seed even from the most infected centres. Duclaux adds that it is no use saying that examination under the microscope is too difficult and delicate an undertaking; Pasteur would reply that he has a little girl of eight who can manage it quite well.

Pasteur asked himself: "Is it that among the eggs of a very much diseased male and female there may be some sound ones? or are some eggs less infected and able to produce grubs which will return to health during culture?" He adds: "I do not know which of these two explanations is the better, and there may be reason in both." Pasteur was already beginning to feel that the facts were not easily reconcilable with the hypothesis of a constitutional disease, and the idea that it might be parasitic was growing in his mind.

The result of an experiment which he had asked Gernez to perform might have enlightened him. During his vacation, which he spent at Valenciennes, Gernez had raised separately four lots, each consisting of forty worms, hatched from eggs obtained from non-corpusculous parents.

The first lot, fed in the ordinary way, produced twenty-seven healthy cocoons, which was quite as good a result as could be expected, considering the climate and the season.

The second lot, fed on leaves moistened with pure water, gave nineteen healthy cocoons. This demonstrated the well-known injurious effect of wet leaves.

The third lot, fed after their third moult on leaves moistened with water containing corpuscles, yielded only four cocoons. Of these one produced a very corpusculous moth; two contained dead chrysalids, of which one was very corpusculous; and in the fourth was a dead worm which had not even reached the chrysalis stage and which was very corpusculous.

The fourth lot, fed like the last, but only after the fourth moult, yielded twenty-two cocoons, six of which were in the state of having scarcely begun the coarse outer fibre, and all were corpusculous with the exception of three which had died in the worm stage, inside their cocoons.

Pasteur's comment on this is as follows: "It is therefore certain that when operating upon young worms, one can attribute a great proportion of mortality to the eating of *corpusculous leaves*; on the other hand, in the case of worms which have passed the fourth moult, and which are therefore relatively more vigorous and have no longer to face the critical moulting periods, mortality does not occur in the worm or caterpillar state; these produce cocoons, but the infection develops in the chrysalids to such a degree that they have difficulty in transforming themselves into moths."

This experiment of Gernez's was a *résumé* of several similar ones. Pasteur again asked himself the question which he had already considered several times: Is the disease caused by a parasite? And he gave a negative reply in a memorandum presented on January 12, 1867, to the *Imperial Committee of Sericulture*:

"(1) Because the disease is certainly constitutional in a great number of cases and precedes the appearance of the corpuscles.

"(2) The eating of corpusculous matter often causes death in young worms without the presence of corpuscles in their bodies.

"(3) I have not yet been able to discover any power of reproduction in corpuscles.

"(4) Their manner of appearance resembles a change of tissue."

"The fact is," wrote Duclaux, "that the corpuscle, instead of multiplying by segmentation or by budding, like bacilli or yeast, can, in certain circumstances, swell itself out into a protoplasmic voluminous mass, the outlines of which are hardly distinguishable, which invades the tissues and permeates them with an almost invisible network in which alone begins a work of delimitation which divides it into distinct corpuscles with definite contours. From the original corpuscle we have thus thousands of identical corpuscles, all sons of the same father. Pasteur had certainly seen this phenomenon of amorphous organization. He had described it with wonderful accuracy, for he was a master observer. He pointed it out to Lackerbauer, who made his drawings, and who tried to produce two plates of it; but he could not explain it, and as he saw that the corpuscle appeared in all the tissues of the diseased worm, he was confirmed in his idea that the malady must be constitutional, and that the corpuscle only announced the stage at which it became visible under the microscope.

4. CAUSE OF THE DISEASE. DEFINITE METHOD OF EGG PRODUCTION.

The breeds of silk-worms most often used, because they yield the finest and most numerous cocoons, allow of only one hatch in each year. There are, however, other breeds, known as *bivoltine* and *trivoltine*, from which two or three hatches may be obtained. Moreover by cultivating mulberry trees under glass, leaves can be produced early enough to begin breeding before the usual season of May to June.

It was thus that Pasteur was able, during the year 1866, to obtain a succession of cultures in little separate groups, in the most hygienic and favourable conditions, and so to obtain a large number of non-corpusculous moths whose seed was sound; and in 1867 he was able to show those who talked of cholera and plague, and of universal and unavoidable infection, that in a *magnanerie* where the disease was rampant, and where whole chambers had died of it, the worms produced from these eggs remained healthy and developed into moths free from corpuscles.

Thus armed, he resumed the experiments in contagion of the preceding year, and found that if a healthy worm is given leaves sprinkled with corpuscles freshly taken from the body of a diseased worm, or from its excreta, the healthy worm is attacked by the corpuscles and soon has all the symptoms of pebrine. The same result ensues if the corpuscles are inoculated by injection. The conclusion to be drawn from this is obvious. Pasteur, revising his former opinion, said: the corpuscles are the only cause of the disease, the cause and not the effect.

Knowing the exact date of an infection artificially produced, one can follow the development of the disease, and see that it is not before the thirtieth day that the worm is so enfeebled as to be incapable of spinning its cocoon. As the existence of the worm does not last more than thirty-five days, and the risks of contagion during the first five days after hatching, whether by injection or by the consumption of corpusculous products, are greatly reduced, it is practically certain that every worm out of a healthy egg will spin its cocoon.

On the other hand, the worm that is already diseased when it climbs the twig, being obliged to spend about twenty days in the chrysalis state, the corpuscles will have time to increase so that they will be contained in the eggs which are produced, and the worms hatched out of these, being infected from birth, will not succeed in spinning cocoons. From this results the double consequence: that worms hatched from sound eggs are not prevented by a subsequent attack of pebrine from giving a good harvest, but that worms hatched out of eggs laid by corpusculous moths certainly are.

The disease is therefore contagious and hereditary. On this point Pasteur gave a hint of great practical value. It is the eggs which ensure the transmission of pebrine, because it is only in the eggs that the corpuscles survive. All those which exist outside, and especially those found in such vast numbers in the dust and on the feeding-trays of the *magnaneries*, inevitably perish in the interval between two seasons.

Pasteur adds: Every process hitherto intended to distinguish good seed from bad has been inadequate and defective, because " all presuppose the existence of the seed, and that it is already either good or bad. That is the fundamental error of all these methods, an egg once laid is always used for breeding. To discover a way of getting sound seed unmixed with bad in all silk-producing countries—that is the problem which we must try to solve."

At the end of the experiments of 1867, Pasteur had solved this problem, and was in a position to give exact instructions to the silk-worm breeders. In order to know whether a particular lot of cocoons are suitable for egg production, as soon as the cocoons are well formed, which will be about six days after climbing the twig, remove about 500 grammes or a kilogramme's weight into a chamber kept at a temperature of from 25° to 30° Reamur. The moths will come out of these cocoons five days earlier than those kept in a temperature of not more than 15°. Every other day, examine twenty of the chrysalids in the warm chamber. If in the course of these examinations you find more than one to be corpusculous, take all the cocoons to the spinning-room, because experience shows that the number of corpusculous ones will increase.

It must be noted that if chrysalids show corpuscles in the first ten or twelve days of their formation, the eggs derived from them will give 40 to 80 per cent. and more of corpusculous worms, because the multiplication of the parasite corresponds exactly to the formation of eggs in the female chrysalis, so that the eggs are infected in greater or less numbers or sometimes throughout. The proportion of corpusculous eggs is much less when the chrysalids in the warm chamber do not show any corpuscles until the fourteenth or fifteenth day after the ascent.

The corpuscles are much easier to discover in moths than in chrysalids, because they are much more numerous. Directly the first moths begin to come out, they should be examined one by one. At least fifty examinations should be made, and more if corpuscles are discovered. In every case where the number of corpusculous moths does not exceed ten per cent., they may be handed over to the egg-laying chamber with the certainty that the eggs will give a result not infected with pebrine.

5. The Spreading of the Disease by the Trade in Eggs.

The method just described has reached the point of perfection, and is now universally employed. At first, however, it encountered much prejudice, injured some interests, and upset long-standing commercial arrangements ; it was not accepted without a struggle. Criticisms, made in good or bad faith, were to be heard on every side ; scientists, such as Joly, the Professor of Zoology at Toulouse, who, having already met Pasteur, ought to have known better, expressed regret that the Government should not have entrusted the study of the prevailing disease to zoologists accustomed to handling scalpel and microscope, to physiologists and doctors initiated into the mysteries of life, instead of to a mere chemist.

The *chemist*, strong in the knowledge of his discovery, defended himself, and as he was inclined to be rather violent in his treatment of adversaries whose good faith was open to suspicion, a few of them came out of the fight with some slight injuries.

Additional irritation was caused him by seeing that these attacks resulted in additional losses to the *magnaniers*, by encouraging them to attempt cultures from eggs which he had condemned as bad ; and he set himself to spread the sound doctrine with an ardour and perseverance which nothing could daunt.

He sent to the breeders and to Maréchal Vaillant of the Silk Commission in Lyons carefully labelled lots of sound and diseased eggs, with a note predicting the result of the hatches in each case, and thus, after having excited curiosity, he gradually induced conviction. He replied to all questions, solved all difficulties. It was enough for him to find a few hints on the customs of egg-producers in the reports of the Agricultural Society of Vigan in order to explain how pebrine had spread all round the world.

In Chapter II of the appendix to the first volume of his *Studies on the Silk-worm Disease*, Pasteur, as an acute psychologist, explains : " Why this scourge has followed the trade in eggs all across Europe and Asia."

This corpuscular disease is of great antiquity, and exists everywhere, although sometimes in an unrecognized latent form which does little harm. When local eggs have not furnished good results, recourse has been had to foreign eggs, which soon in their turn become contaminated. " In order to concentrate our ideas on the point which is now occupying our attention, let us imagine a very prosperous sericultural locality, such, for example, as Adrianople in Roumelia in 1856. There, as formerly in France, breeders themselves produce each year the seed which they require. They make inquiries as to the best cultures in their neighbourhood, and buy a few kilogrammes of cocoons for seed. Anyone who has a very satisfactory *chamber* becomes the purveyor of good cocoons to all his friends and acquaintances. They only raise one strain of seed.

"These are the normal conditions of sericulture, and this was the situation in our sericultural departments before the advent of the scourge. It was only a few big *magnaneries* of twenty to thirty ounces or more which did not produce their own eggs. They were bought in little *chambers*, and placed preferably in mountainous localities where the air was fresher and drier than in flat country. In these circumstances there was, properly speaking, no real trade in seed. The sale price of it in France in prosperous times never rose above three francs the ounce of twenty-five grammes.

"Now let us imagine the arrival in the happy and prosperous part of Roumelia, which we have taken as an example, of persons sent from France and Italy by the breeders in districts where there is a lack of good seed. These agents begin by establishing themselves in the centre of a fairly large district; they then buy the seed brought to them at prices naturally much higher than those which have hitherto obtained in the neighbourhood. There has not been time to make sure whether the *chambers* which have produced these cocoons have done well or badly. The peasant, allured by the thought of gain, declares that the cocoons which he offers come from the best strains that can possibly be seen. In spite of all this our egg-dealers usually obtain in the first year seed which is on the whole of very good quality, and gives their employers entire satisfaction.

"Consequently those who have bought the Adrianople seed, and all the other breeders in France, are full of its praises, and everybody tries to procure it. Our dealers, followed by many imitators, hasten back to this happy country the following year. They had arranged for 1,000 ounces of seed, but countless orders oblige them to bring back 10,000 and more. They had gone out the first year as agents of Agricultural Societies, or subscribers, who paid their expenses, and who made it a condition that the imported seed should be sold at a comparatively moderate price, fixed in advance. This time, sure of the sale of all the seed they can obtain, they are careful to keep a free hand. They go at their own risk, and are no longer mere agents, but independent dealers in search of goods which they will sell to the best possible advantage on their return, without any control as to quality.

"Changes of another nature have meanwhile taken place in our country of successful seed production. It is already known that the buyers from France and Italy will return. They have said so. They have even made bargains in advance, foreseeing that there is a fortune to be made out of their new trade. Under the influence of this knowledge a great transformation has begun in the neighbourhood of Adrianople. Each breeder wants to increase the size of his harvest. Into a chamber where only an ounce of seed was raised before, he now puts an ounce and a half or two ounces. Less care is taken in the culture, and causes of infection increase, so that the pebrine, hitherto latent, develops slightly. The proportion of corpusculous moths increases.

"As for our dealers, they are able to make even fewer inquiries about the quality of the cocoons and the details of the culture which had produced them than in the preceding year. All the seed brought to them is accepted for breeding purposes. Each time the new seed gives good results in France and Italy, and the demand for Adrianople seed increases yet more in the following season. Our dealers therefore appear a third time, and again with numerous imitators.

"On their side the breeders in our supposedly healthy locality keep on increasing the size of their hatches, the pebrine consequently develops more and more, till at last, at the fourth or fifth season of this uncontrolled bought seed, Roumelia finds itself thoroughly infected with the corpuscle disease. From this time seed brought from Adrianople produces nothing but failures. What matter? Our dealers simply carry their operations further afield, where the same causes bring about the same results, and it is thus, in my opinion, that the trade in seed has brought about not the introduction of the disease, but its increase and its virulence."

6. FLACHERY DISEASE.

At the beginning of 1867 Pasteur had distributed, in as many small lots as possible, the seed prepared during the preceding season, the soundness of which he could guarantee. Success was general. "Nevertheless," wrote Duclaux, "as the letters announcing the result of the cultures arrived, our master became more and more troubled. He kept his thoughts so hidden from us that we could not understand his anxiety, until a day when he suddenly appeared before us, almost with tears in his eyes, and sinking disconsolately into a chair, cried: 'I have achieved nothing—there are two diseases.'" It was the rending of a veil.

Pasteur had just learnt that in different places and different climates, and at different dates, cultures from sound seed had nearly all failed. He had already observed similar but apparently accidental occurrences with seed of uncertain origin, but, believing like everybody else that there was but one disease, he had not realized their significance.

Among the reasons which he had given to the Imperial Commission on Sericulture for not believing in the parasitic origin of pebrine, two were particularly important: in a great many cases the disease precedes the appearance of the corpuscle, and on the other hand the eating of corpusculous matter often kills the worms without producing corpuscles.

The fact is that there exists a special disease called *flachery*, or the disease of *flaccid death*, less common than pebrine, and often associated with it. Pasteur had seen one case of this association in the first days of his first season in 1865. Some corpusculous worms had succeeded in spinning their cocoons, and had given a good harvest, because they had been infected during the worm-stage of their existence, but too late for the corpuscles to be very highly developed; at the same time some non-corpusculous worms died, these having died of flachery. In 1866, Pasteur had tried to give pebrine to worms by feeding them with leaves washed over with the pounded remains of very corpusculous moths and worms: the worms fed thus died of flachery without the appearance of any corpuscles.

Now the difference between the two diseases was proved by the evidence, and this was already an important result. Pasteur saw light on many points which had been obscure in his memorandum and in the notes which he had taken on his experiments.

In the first place flachery was hereditary. Many seeds free from corpuscles, belonging to the same strain, divided among several breeders and treated in different ways, and often in places far from one another, had produced worms attacked by the same disease at the same age and in the same manner; this could only be explained by the simultaneous development of the same germ. The time was generally after the fourth moult, at the moment when the healthy worm becomes enormously voracious, other worms were seen to refuse food, drag themselves languidly about, and then die. Usually almost immediately after death the bodies became soft and soon decayed, at other times they remained firm and hard as if mummified. If the disease developed very late the worm might still be able to climb up the twig and, according to its condition, either spin a perfect cocoon, or die after having wrapped itself in a sort of rough fibre through which its corpse could be seen.

Pasteur had not made notes of the behaviour of every lot of worms from which eggs had been obtained, but he remembered with regard to one lot, the descendants of which had died of flachery, that the worms had presented a languid appearance at the moment of climbing the twigs, and this had made him hesitate about using their moths. He had decided to do so, however, and, on finding that the moths contained no corpuscles, had kept their eggs.

This observation, by opening new perspectives, gave him back his courage. He sought out cultures attacked by flaccid disease, obtained eggs from them, and assured himself that the moths contained no corpuscles. At the first trials in 1868 this seed gave disastrous results; the worms were reared with great care, in separate lots, but nearly all succumbed to flachery, and Pasteur concluded from this that; "there is no longer any doubt that the disease of flaccid death can be hereditary, and can attack a chamber quite independently of all methods of hatching the eggs, of airing the chamber, or of the excess of heat or cold to which the worms may be subjected, all conditions which may accidentally increase this same disease. From this may be seen the urgent necessity of never obtaining eggs, however satisfactory the outward appearance or the microscopic examination of a moth may be, from chambers in which any worms have shown langour between the fourth moult and the twig-climbing, or in which many have died at this stage of flachery. I insist again, and with even more emphasis than last year, upon this recommendation."

7. Deductions for Human Pathology.

Pasteur's researches on silk-worm diseases had now given all the essential results. He continued them, however, from 1868 to 1870, in order to verify certain points of detail, to reply to objections, to convince those who still hesitated, and to spread the knowledge of a method in which he saw an important element of national prosperity.

Pasteur easily demonstrated that flachery disease has this one point in common with pebrine, it is contagious. In contrast to the excreta of a worm in perfect health, which are hard and dry like little seeds, those of the diseased worm are soft and sticky, and adhere to the leaves over which the worm has passed. It is enough to give these soiled leaves to healthy worms to make them become diseased; but the injected or ingested corpuscle develops outside the intestine and after an interval of time which never varies, whereas the flachery germ has its seat in the digestive canal, and can prove fatal in a few hours or a few days, being then known as worm typhus or cholera; or it may last three weeks or more, because there is always a certain number of worms capable of resisting it, and it is very seldom that a chamber attacked by the flaccid-death disease is entirely destroyed. In the case of this disease worms present an individual power of resistance which varies considerably. Pasteur thus recognized for the first time the possibility of susceptibility.

The germs of flachery multiply in the intestine; they are found in the stomach of the moth in the form of micrococci in pairs or in chains, and as vibrions with or without bright nuclei—these nuclei being the extremely resistant spores by which the species propagates itself. If the examination of the stomach is negative, the seed may be considered sound. Unlike the germs of the corpuscles, the germs of flachery are free and widespread, and the disease can appear spontaneously. Bray some mulberry leaves in a little water, and, at a temperature corresponding to that of the summer season, when the mulberry leaves appear, microbes will develop similar to those which swarm in the intestines of the flaccid worms. Sprinkle this pulp on the leaves given to healthy worms and they will die of flachery after a certain time, for instance eight to fifteen days. Worms thus infected may cause a fresh infection which will result in a disease identical in nature, but more rapid in development, being fatal in from six to eight days. Pasteur thus acquired the idea of an increase of virus by passage through an organism.

He made parallel studies in worms infected by the ingestion of soiled leaves and by direct inoculation through a prick, and the difference in the development of the malady in the two cases revealed to him the influence of the *mode of entry.*

Another serious question which is also connected with many human diseases, is this: the germ of flachery is common and found everywhere; why does it not always develop? Here Pasteur recognized the double influence of the *seed* and the *soil*; everything which increased the strength of the one and the susceptibility of the other could determine an epidemic. The worm constantly takes in with the leaf germs which the digestive juices are capable of destroying; but if the leaf has been damped, if it has fermented before being eaten, the damaged food will contain more numerous and more active germs which the digestive juices will no longer entirely destroy. On the other hand, even when the quality of the food is good, and the number of germs does not exceed the normal figure, the worm's power of resistance may be weakened by stormy weather, by an excessively high temperature, by bad ventilation, or by poisoning caused by the braziers used by many breeders.

Finally, the weakening of the organism may be due to hereditary tendency, the parents being themselves infected and having transmitted to their descendants a diminished vitality and increased susceptibility.

"It is thus," writes Duclaux, "that Pasteur, at the conclusion of his researches, found that he had not only solved the problem which he had set himself of the revival of sericulture, but had also placed upon an experimental basis the great questions of contagion and heredity which dominate the whole of pathology."

CHAPTER XIII

BEREAVEMENTS

In the course of this long and arduous campaign, during which Pasteur only abandoned his studies on silk-worms in order to return to his previous work, fate had dealt him a succession of blows in the death of several of his nearest and dearest. He had already lost his mother, and then his eldest daughter, Jeanne, who had died of typhoid fever in the little house at Arbois. In 1865, just after he had established himself at Alais, he was summoned to his dying father, and arrived only in time to follow the coffin to the cemetery.

That evening he wrote to his wife and children: "Poor grandfather is no more. He died on the day of your First Communion, dear Cécile, and these two memories will live together for ever in your heart, my dear child. I had a presentiment of what was about to happen, when on that morning, at the very moment when he received the blow from which he was never to recover, I asked you to pray for the grandfather of Arbois. Your prayers must have been acceptable to God, and who knows whether grandfather himself was not aware of them, and was not rejoicing with poor little Jeanne over the pious fervour of Cécile!

"All day I have been going over in my mind the marks of affection shown me by my poor father. For the last thirty years I have been his first and almost his only interest in life. I owe everything to him. When I was young he kept me out of bad company, made me acquire the habit of industry, and gave me the example of an upright and well-filled life. This man was in distinction of mind and character far above his position as judged from a worldly point of view. He made no mistake about it, he knew that it is the man who dignifies the position, and not the position the man. You, dear Marie, did not know him in the days when he and my mother worked so hard for the dear children whom they loved so well, and especially for me, the one whose books, whose months at college and whose board and lodging at Besançon cost them dear. I can still see him, my poor father, in the few leisure moments left him by his manual work, reading much, always educating himself. . . .

"And the most touching thing about his affection for me is that it was never mixed with ambition. You will remember that he would have been quite content to see me head of the college at Arbois. This was because he saw beyond my possible advancement the work which would be necessary to procure it, and beyond the work the possible injury to my health. And nevertheless, being what he was, and what I realize him now to have been, some of the successes of my scientific career must have filled him with pride and joy. It was his son, his name. It was the child that he had guided and advised. Oh! my poor father! I am indeed happy to think that I gave you some satisfaction."[1]

In the month of September of the same year he lost his youngest daughter, Camille, who was barely two years old, and in the month of May, 1866, his daughter Cécile, aged twelve and a half. Of the five children who had been the joy of his home, he had only two left. Under his rather rough exterior he had a most tender heart; the only alleviation he found in his sorrow was through increased devotion to the work of which the population of the south was already appreciating the value.

His labours counted for nothing, and he never considered his own personal interest.

In the summer of 1865 he had been one of the guests of Napoleon III in the palace of Compiègne, and when the Emperor asked him why he reaped no benefit from discoveries which were enriching the world, Pasteur replied: "In France scientists would think themselves dishonoured by acting in such a way."

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[1] Quoted by René Vallery-Radot, *op. cit.*, p. 145.

He wrote in the preface to his *Studies on Silk-Worm Disease*: "It is the glory of the man of science to esteem discoveries which at their birth can only be appreciated by his equals far above those which immediately win public favour by instant application; but in the face of misfortune it is equally glorious to sacrifice everything in order to try and be of assistance."

Pasteur carried disinterestedness so far as to take at his own expense the steps to prevent clever manufacturers from turning his discoveries to their own profit and the detriment of the public.

When, after his communication of February 10, 1862, on the subject of the part played by mycoderms in acetic fermentation, he made known to the Academy of Science his *New Industrial Method of Fabrication of Vinegar*, he was careful to give in a note the following warning:

"As it often happens that scientific principles published by their discoverers are made use of by others, with the addition of apparatus or some insignificant modifications, for obtaining patents of invention, I have, by the advice of competent persons, and before making my communication of February 10th, taken out a preliminary protection forestalling the patenting of all inventions to which my work may give rise, and I add that I am resolved to let this lapse from to-day for the benefit of the general public."

CHAPTER XIV

PASTEUR PROFESSOR OF CHEMISTRY AT THE SORBONNE—FOUNDATION OF A LABORATORY OF CHEMICAL PHYSIOLOGY

On July 1, 1867, Pasteur was summoned to Paris, where he was to receive a prize awarded to him by the Exposition Universelle for his studies on wine. A short time after this an incident occurred at the École Normale which put an end to his career as Administrator.

The students addressed a letter to Sainte Beuve congratulating him on having defended in the Senate "liberty of thought, so often misrepresented and attacked. Much courage is required," they said, "to address the Senate in favour of independence and freedom of thought." This letter was published and Nisard, Director of the school, expelled the pupil who had signed this document on behalf of his comrades.

This drastic treatment caused great excitement, which spread from the school into university circles, and even among the general public. The pupils demanded the immediate reinstatement of their comrade. Pasteur wished to intervene to quiet things down, but he had not the diplomatic gift of conciliatory speech; it was difficult for him to overlook a breach of discipline, and before the hostile attitude of one section of students he retreated. All the pupils left the school. It was a miniature revolution.

The *Moniteur* of July 10th announced that in face of such disorder the authorities ought immediately to have broken up the school. It would now be entirely reconstituted, and would reopen on October the 15th.

The School was, in fact, reconstituted. The Director, Nisard, was replaced by Francisque Bouillier, and Pasteur by one of his best friends, Bertin, who had been his colleague in the Faculty of Strasbourg. Pasteur was nominated Professor of Chemistry at the Sorbonne, taking the place of his former master, Balard.

He took advantage of his new appointment to ask the Emperor to found a laboratory of chemical physiology. "Sire," he wrote, "my researches on fermentations and on the part played by microscopic organisms, have opened to chemical physiology new fields from which agricultural industries and medical science are already gathering the fruit, but a vast area still remains to be covered. My greatest delight would be to explore it with fresh ardour unhampered by the lack of practical means.

"When it is a case of discovering, by a patient scientific study of putrefaction, some principles which may help us to discover the causes of gangrenous or contagious disease, I should wish to find, in the outbuildings of a fairly spacious laboratory, a place where experiments could be undertaken with ease and without danger to health.

"How can one devote oneself to researches on gangrene, on virus, or to experiments in inoculation, without a proper place in which to receive animals, dead or alive? Butcher's meat fetches an exorbitant price in Europe; it is a drug in the market at Buenos Ayres. How, in a tiny cramped laboratory, can one test the processes by which its preservation and transport might be made possible? The disease known as *sang de rate*[1] causes the district of the Beauce an annual loss of four million francs; it would be necessary to go there for several years in succession, no doubt at the hottest season, and to spend some weeks in the outskirts of Chartres, in order to devote oneself to the minutest observations.

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[1] Lit., *blood of spleen*, a name given to anthrax, apparently in allusion to its effect upon this organ. [Trans.]

"These investigations and a thousand others corresponding in my opinion to the great transformation of organic matter after death, and the return of all that has lived to the earth and the air, can only be attempted in a vast laboratory. The time has come to liberate experimental science from the poverty which shackles it"[1]

The Emperor gave his consent. The Minister Duruy, who had a high opinion of and a real friendship for Pasteur, supported the project to the utmost of his power. The future laboratory was to be constructed on a site between the little rectangular lodge and that of the porter, in the court-yard of the École Normale and the houses of the Rue des Feuillantines.

At the end of the year Pasteur learnt that the Board of Public Works had refused the necessary credits for the commencement of the building. He was furious, for it was just at this time that millions were being thrown away on the construction of the sumptuous Opera House of Charles Garnier, and he wished to make the general public judge of the matter. He pleaded his cause, which was that of all men of science, in an article entitled *The Budget of Science*, which was published by the *Revue des Cours Scientifiques*. "Laboratories and discoveries," he said, "are correlative terms. Suppress laboratories and the physical sciences represent only sterility and death. They will no longer be anything better than mere text-book sciences, limited and powerless, and not sciences of progress and promise. Away from their laboratories the physicist and the chemist are like unarmed soldiers on the field of battle."

Pasteur ended by winning the day, and in April, 1868, he saw, to his great joy, the commencement of the work.

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[1] Quoted by Vallery-Radot, *op. cit.*, p. 205.

CHAPTER XV

PASTEUR'S ILLNESS

At the beginning of September, 1868, Pasteur left for Toulon, where he was to assist at the experiments to be made, by command of the Admiralty, in heating wine. He wrote to his pupil Raulin: "Large quantities of heated and non-heated wine are to be sent off to Gaboon and Cochin-China, so as to test the process. Our crews in the colonies drink nothing but vinegar."

In October Pasteur returned to Paris, full of plans for his course of lectures at the Sorbonne, for the organization of his laboratory, and for the season of 1869 in the south, for which he was already preparing. The last season had, however, greatly fatigued him. He was still suffering from the effects of the excess of work which he had undertaken, and especially from the long excursions he had made under a broiling sun to visit different *magnaneries*, and from the lengthy sojourns in overheated rooms.

On October 19th he was to present to the Academy of Science a thesis written by Salimbeni, an Italian scientist, who had been experimenting for a long time with the new method of sericulture, and who set forth the splendid results he had obtained. Pasteur was unwell that day; he had a tingling sensation all down his left side, and after lunch had a fit of shivering; nevertheless he would not give up going to the Academy. In the evening, after a light supper, he went upstairs and was almost immediately seized with apoplexy. He could not speak, and his left side was paralysed; for a whole day death seemed imminent. René Vallery-Radot has given an account of these sad hours: "One friend after another visited the room in the École Normale. One of the first was Henri Sainte-Claire-Deville. To him Pasteur said sadly: 'I am sorry to die; I should have liked to render further services to my country'; and Sainte-Claire-Deville, hiding his grief under an appearance of confidence, replied: 'Cheer up, you are going to get well; you will make a great many more wonderful discoveries, and spend many more happy days. You will survive me, I am older than you are, and you must promise to make the oration at my funeral. I want you to, because I know you would speak well of me,' he added, between smiles and tears." Both prediction and wish were to be realized.

After a few days of terrible anxiety the danger seemed passed. One night, when his pupil Gernez was sitting up with him, Pasteur dictated a note indicating a means of discovering, by early tests, whether silk-worm eggs were disposed to flachery; and to the great astonishment of Gernez this note was so well thought out and so well expressed, that it could be published without any alteration in the report submitted to the Academy on October 26, 1868.

As soon as Pasteur's illness became known, work on the building of his laboratory ceased. Pasteur was much upset on hearing of this stoppage, which was no doubt ordered by some official, who anticipated his immediate death and wished to save the erection of buildings which would not be needed. The Emperor, on being informed, ordered the continuation of the work.

Pasteur's convalescence was slow, but steadily progressive. By the end of December he could walk a few steps without assistance. In January, 1869, he made the journey from Paris to Alais, where he wished to superintend some early cultures. In November he established himself near Trieste, at the Villa Vicentia, belonging to the Prince Imperial. There he was to direct the culture of a hundred ounces of seed, by which, in a district where silk-worms had long ceased to be a source of profit, the value of his method should be conclusively proved. It was there that Pasteur wrote most of his *Studies on Silk-Worm Disease.* He might well have given at the end of his book the results of this season: the harvest of cocoons sold for 27,000 francs; expenses of every kind had not exceeded 5,000 francs.

CHAPTER XVI

WAR OF 1870

Pasteur returned to France in July, 1870, by way of Munich, where he paid a return visit to Liebig in his laboratory. The great chemist received him with the utmost courtesy, but refused all discussion of subjects on which they disagreed. His state of health, he said, did not permit his keeping up an argument. A few days later war was declared.

Pasteur being still partially paralysed, felt himself useless in Paris, and withdrew to Arbois with his wife and daughter. His son, aged eighteen, had enlisted. From the little house which had been his father's, he followed the disastrous struggle with the keenest interest.

He read the protest of Chevreul at the Academy of Science, denouncing the bombardment of the Natural History Museum, and wishing to associate himself with it, he returned to the Dean of the Faculty of Bonn the diploma of Doctor of Medicine which had been awarded to him, in 1868, by the University of that town in recognition of his having: "by his far-reaching experiments, contributed more than anyone else to the history of the generation of microscopic organisms and had wonderfully advanced the science of fermentations."

In the letter dated January 18, 1871, which accompanied the diploma he said: "The sight of this parchment is now hateful to me, and I feel it an insult to have my name, which you have qualified with the title of *virum clarissimum*, associated with one doomed from henceforth to the execration of my fellow-countrymen, that of *Rex Gulielmus*.

"While loudly proclaiming my respect for you and for the celebrated professors who have appended their signatures to the decision of the members of your body, I obey the voice of my conscience in asking you to erase my name from the archives of your Faculty and to take back this diploma as a token of the indignation inspired in a French scientist by the barbarity and hypocrisy of one who, in order to gratify his criminal pride, persists in the massacre of two great nations."

A few weeks later Pasteur received this reply from Bonn:

" Sir,

The undersigned, Dean of the Faculty of Medicine in Bonn, is charged with replying to the insult which you have dared to offer to the German nation in the sacred person of its august emperor, King William of Prussia, by sending you the expression of *his greatest contempt.*

Dr. Maurice Naumann.

P.S. Wishing to preserve its archives from pollution the Faculty returns herewith your libel."

Pasteur replied:

" I have the honour to inform you, Mr. Dean, that at the present time an expression of contempt from the lips of a Prussian subject has, to a true Frenchman, a value equal to that of *virum clarissimum* with which you formerly described me in your official archives."

Pasteur reflected deeply on the causes of the French disasters, and he attributed them mainly to a mistake which he had often pointed out. He said in an article published on March 20, 1871, in the *Salut Public* of Lyons: " The mistake which has prevented France from finding men capable of turning her resources and the bravery of her children to account, is that which she has made in dissociating herself, for the last half-century before this terrible year, from all great intellectual work, especially from that performed in connection with physical science." And he showed how Lavoisier, Chaptal, Berthelot, Monge and others had discovered ways of manufacturing arms and munitions which would have enabled our soldiers in 1792 to save their country.[1]

"He was longing," writes Duclaux, "to get back to work, to play his part, which he knew was already a great one, in the lifting up of his stricken country. He already dreamt of a Pasteur Institute, where he could be surrounded by all his assistants, and where he could lead them to fresh triumphs. 'My head is full of the most splendid plans,' he wrote to me on March 29, 1871. 'My brain has been lying fallow through the war. Now I am ready for a fresh crop. Alas! perhaps I am deluding myself; but in any case I shall make the attempt. Oh! why am I not rich, why am I not a millionaire! I would say to all of you, Raulin, Gernez, Van Tieghem, etc.: Come! we will transform the world with our discoveries! How lucky you are to be young and well! Oh! why can't I begin my life of study and work over again. Poor France, dear country, why cannot I help to raise you up again from your misfortunes!'"

Some Italians who admired Pasteur's work and who took a very gloomy view of France's future, offered him the directorship of a laboratory in Milan or a Chair of Chemistry at Pisa. He refused. "I should consider it a crime," he said, "and deserving the penalty of desertion, if I were to seek away from my unhappy country, a situation better from a material point of view than that which she can offer me."[2]

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[1] These reflections of Pasteur have lost none of their interest. During the Great War science has rendered the same services as in 1792. To give only one example: in 1914 chemical industries were far more developed in Germany than in France. The Germans had secretly prepared their asphyxiating gases and reckoned on our being without defence against this new weapon. Had their hope been realized our defeat would have been inevitable; but our scientists first gave us efficacious means of protection, and then fabricated the gas and created the machines with which we beat the Germans in this field of chemistry where they thought themselves supreme.

[2] Quoted by René Vallery-Radot, *op. cit.*, p. 286.

CHAPTER XVII

STUDIES ON BEER

Pasteur had accepted an invitation to go with his family and spend some time with his "dear Duclaux," who was then Professor of Chemistry at Clermont-Ferraud.

At Chamalières, near Clermont, there was a brewery which reminded Pasteur of the distilleries of the north and of his first studies on fermentation. German beers were incontestably superior to French and enjoyed a European reputation. Would it not be possible to make them just as well in France and so take an initial revenge in the field of industry? The *Studies on Beer* originated with this double motive.

Pasteur's object was fully accomplished, and the improvement in French brewing is mainly due to his work. His book, developing the theory already put forward in his *Studies on Wine*, proves that diseases of beer are due to parasites counteracting the effect of the pure yeast which alone can produce good fermentation. He was able to repeat what he had already said: "In all these investigations, if one loses sight of the existence of microscopic beings, one sees only what is extraordinary, and imagines that one is in the presence of special creations, whereas in fact, here as everywhere else, general laws are finding quite simple and natural applications."

In September, 1871, Pasteur went to London to visit the great English breweries: the use of the microscope was unknown there. He showed the amazed brewers the micro-organisms which announce by their number an alteration which is taking or has already taken place.

He made the same demonstration to the brewers of Tantonville, near Nancy.

In order to obtain sound beer, it is sufficient to protect it from the germs of disease during manufacture and to put it into barrels which have been cleared of germs. This is the last chapter and the conclusion of the *Studies*.

CHAPTER XVIII

QUESTION OF THE TRANSFORMATION OF SPECIES

Beer can be sound without being pleasant to drink. There is a delicate question of flavour and of individual taste; Pasteur, who did not like beer, took but a slight interest in this question, and often wandered from it. Thus one finds in his books, chapters only remotely connected with brewing, as, for example, his discussion with Trécul on the subject of micro-organisms which possess the property of transforming themselves one into the other.

Trécul, in accordance with several other learned botanists, believed in this transformation. Pasteur denied it. He had showed in his works on fermentations that the germ is specific: each fermentation has its ferment. Darwin and his school, however, argued on the other side, and the heterogenesists, fortified by this support, affirmed with all the more ardour the mutability of species.

Pasteur himself had thought he saw the mycoderm of wine being transformed into alcoholic ferment, and with perfect sincerity had pointed out this result of an experiment which alone contradicted a doctrine which he had established by innumerable others.

He sowed some mycoderm on beer-wort contained in a flat porcelain dish. The mycoderm developed and formed the usual *veil* on the surface of the wort. He then broke up the veil and submerged it by violently shaking the liquid; he then poured the liquid into a flask with the cork pierced by one end of a glass tube, the other end of which was under water. Flask and tube were completely filled so that the wort was isolated from contact with air. As a matter of course all the manipulations were performed with the greatest care, so that no germ other than the mycoderm should be developed in the liquid. Pasteur saw a fermentation set up which appeared to be due to cellules of mycoderm transformed into cellules of yeast. He related in his *Studies on Beer* how he perceived his mistake.

"In experiments performed in the manner which I have just described, the yeast, which appears and which promptly sets up alcoholic fermentation, is originally carried in atmospheric air, which lets the germ fall either on the mycodermic veil or on the objects which are used in the series of manipulations. Two peculiarities of these experiments enlightened me as to this cause of error. I sometimes found, at the bottom of the flasks where I had submerged the *fleur*, among the cellules of mycoderm, some large spherical cellules of *mucor mucedo* or *racemosus*, these yeast-cellules which we were soon to get to know in studying this curious mould. Since *mucor mucedo* or *racemosus* is to be found where I have only sowed mycoderm of wine, then, I said to myself, one or more spores of this *mucor* must have been carried by the movement of the air. Now if the air introduces spores of *mucor* into my experiment, why not also cellules of yeast, especially in my laboratory.

"Furthermore, it happened that in multiplying experiments under the pressure of my uncertainty, and in constantly seeking this desirable transformation which fitted so well into the physiological theory of fermentation which I had formed, I had some negative results, that is to say, that the transformation of the mycoderm into yeast did not take place although all the conditions appeared just as favourable as in the experiments which had succeeded. Why, I wondered, this inactivity in the cellules of the mycoderm ? Even in the most favourable cases of supposed transformation, it no doubt happened that innumerable cellules of mycoderm did not become cellules of yeast ; but how could one admit that among all the hundreds of thousands of submerged cellules, all could be incapable of this transformation if the transformation were really possible?

"It was then that, in order to extricate myself from the difficulty, I resolved to alter the procedure in these tests, and to apply to the investigation that I had in view, a method of culture which would entirely, or almost entirely, avoid the only cause to which I could imagine my error to be due, that is to say, the possible failure of the cellules of yeast during manipulation."

A new and surer method was devised, and "I never again," said Pasteur, "saw yeast or alcoholic fermentation follow on the submersion of the *fleurs*. . . . At a time when the idea of transformation of species is so easily adopted, perhaps because it dispenses with rigorous experiment, it is not without interest to consider that in the course of my researches on the culture of microscopic plants in a pure state, I thought one day that I had reason to believe in the transformation of one organism into another, namely the transformation of *mycoderma vini* or *cerevisiæ* into yeast, and that on this occasion I was mistaken; I had not known how to avoid the illusion which my reasoned belief in the theory of germs had so often led me to discover in the observations of others."

CHAPTER XIX

ALTERNATION OF AEROBIC AND ANAEROBIC LIFE — PHYSIOLOGICAL THEORY OF FERMENTATION — PASTEUR AND CLAUDE BERNARD

Bail, a learned German botanist, studying *mucor mucedo*, had shown in 1857 that this mould is able to live on the surface of a sugar solution in contact with air, and under these conditions it destroys the sugar and gives off carbonic acid; but it can also exist submerged in the solution, protected from air, and then sets up quite a brisk alcoholic fermentation. When living on the surface it develops a fine network of mycelial filaments; when it is submerged the spores increase in size, the mycelial tubules which arise from them are stouter and shorter than in the normal plant; they bud and form globules in chains which resemble the cellules of beer-yeast, which Bail considered them to be.

Pasteur made the same experiment and found it perfectly correct. Bail's observation was right, but his interpretation wrong. "Deprived of oxygen, or having available after a life of activity an insufficient quantity, the mucor can still live without the direct action of this element and the changes that it excites; but in this case all the changes of an alcoholic fermentation can be observed, that is to say a definite proportion of sugar, related to the solid matter assimilated and fixed by the plant, is decomposed into alcohol and carbonic acid, a decomposition which continues so long as life remains in the submerged cellules. Fermentation ceases absolutely, or at least gives so little external evidence of its existence as to be imperceptible and all vital activity vanishes from the cellules, which appear old, worn out, distorted in outline, and full of granules. But life, if suspended, is not extinct: it is only an apparent death. Restore oxygen to the plant and allow it to live again under the action of this gas, and growth will begin again and once more become capable of setting up fermentation for a short time even when deprived of air.

"Oxygen here shows itself endowed with a force capable of stimulating nutritive actions which can afterwards continue away from its influence; but the energy which it has imparted to the vital activity of the cellules, is gradually used up."

When one renews the activity of the submerged plant with free air, the globules so closely resembling those of yeast, are seen to reproduce the *mucor* with all its ordinary characteristics. Bail was therefore wrong in fancying this a transformation of species; the plant had only changed its form, to adapt itself to the new life, and this change of form was accompanied by alteration of functions.

Pasteur had observed analogous facts in the submerged mycoderm of wine. This vegetable growth, so little like the mucor in its external characteristics, resembles it in its properties. The power of separating sugar into alcohol and carbonic acid, that is of fermentation, is only, therefore, an accidental property, which appears under certain conditions of existence and disappears under others.

Thus mucor and mycoderm, normally aerobic species can adapt themselves to life without air. Other organisms, such as beer-yeast, normally anaerobic, are capable of presenting the opposite property. It is interesting to notice how these organisms react when the medium in which they are living, originally deprived of air, is gradually aerated.

If one sows a few yeast cellules in a liquid artificially deoxygenated, they can be seen developing slowly and producing a feeble fermentation. When the fermentation has ceased, one finds that a small amount of yeast has decomposed a considerable amount of sugar; a gramme of yeast will correspond to a transformation into alcohol and carbonic acid of from 150 to 200 grammes of sugar.

If one plants yeast in a sugar solution containing dissolved oxygen, it develops more actively; the transformation of 60 grammes of sugar is sufficient to produce a gramme of yeast.

If one supplies still more oxygen to the yeast, as, for example, by planting it in a liquid freely bathed with air spread out in a thin layer over a wide surface, fermentation will be still more rapid, combustion will be complete, the sugar will no longer form alcohol but only carbonic acid, and it will be sufficient to destroy four or five grammes of it in order to produce a gramme of yeast.

Thus anaerobic species can adapt themselves to life in contact with air, and aerobic species to life without air; but it is always during life without air that alcoholic fermentation manifests itself.

Arrived at this point in his investigation, Pasteur did not hesitate to affirm that: "the production of alcohol and carbonic acid by means of sugar, that is to say alcoholic fermentation, are chemical actions bound up with the vegetative life of cellules of widely different kinds, and that these appear when the cellules are no longer able to consume freely, as a result of respiration, the materials required for their nutrition, in other words by the absorption of free oxygen gas, and that they go through life using up oxygenated matters which, like sugar and explosive substances, produce heat on decomposition. The *ferment* power we thus see is not peculiar to certain beings or organisms, but is a general property of the living cell, a property always ready to show itself, and actually appearing as soon as life is no longer carried on under the influence of free oxygen, or of a quantity of this gas sufficient for the complete process of nutrition."

Pasteur expressed what he called the physiological theory of fermentation in this concise form: "fermentation is the result of life without air."

Claude Bernard towards the end of his life viewed the phenomena differently. When he died, on February

10, 1878, his assistant, d'Arsonval, found among his papers some notes which his friends thought it their duty to publish, pointing out at the same time that they were, as Paul Bert expressed it, " incomplete notes and confidences which a great mind had made to itself while seeking a path by which to arrive at that certainty which, in the case of men of genius, sometimes precedes proof, marking out the way indistinctly with hypotheses and facts."

Some sentences directly contradicted Pasteur's doctrine of alcoholic fermentation. Were these conclusions justified by experiments, the details of which were not given, or were they simple suggestions which should have been tested by subsequent experiment ? There was no means of knowing.

Pasteur was much chagrined by this posthumous publication. He had held Bernard in high esteem and had been on most friendly terms with him for a long time. When Claude Bernard in 1866 was so ill that hope of his recovery was abandoned, Pasteur published in the *Moniteur Universel* an article in which he analysed his friend's discoveries, pointed out their importance, and proclaimed his admiration for the magnificent work of this scientist who was, in the words of J. B. Dumas, more than a great physiologist, physiology itself. Claude Bernard read this article during his convalescence, drew from it new confidence and strength, and was greatly touched by the delicate feeling which had inspired it.

Pasteur had often met his friend at the Academy of Science during the last months of 1877; they had had long conversations and no reference had been made to the subject which now seemed to divide them. One might of course consider that these *Notes* expressed the considered opinion of their author. " This view, however," wrote Pasteur in his *Critical Examination of a Posthumous Work of Claude Bernard*, " leaves the enigma of his silence towards me unsolved ; but why should I seek for any explanation other than that which an intimate knowledge of his noble character suggests ? Was not this silence a fresh witness to his kindness and one of the results of the mutual esteem which united us? Since he thought that he held in his hands the proof that the interpretation which I had given to my experiments was erroneous, did he not wish to wait to tell me of it until he believed himself ready for a definite publication? I like to attribute exalted motives to the actions of my friends, and I wish to believe that the surprise which his reserve towards the colleague most interested in his contradiction has caused me, ought to give place in my heart to sentiments of pious gratitude.

"In any case Bernard would have been the first to remind me that scientific truth ranks above the conventions of friendship, and that it is now my duty to discuss in my turn and with perfect freedom his views and opinions."

Duclaux has, with his usual raciness, given a brilliant account of this controversy, which was carried on by Bertelot in support of Claude Bernard's thesis. "It was," he says, "truly a curious encounter, but as it produced no new facts it has lost interest. Pasteur emerged from it with his ideas more firmly fixed, and M. Bertelot with the appearance of having given up none of his. This should make us distrust all discussions, even scientific ones.

"One fancies that a scientific discussion is more likely than another to lead to something, because it keeps within the region of facts; but a fact, even of a physical nature, is nothing in itself. It only becomes something when it is stamped as an intellectual fact by the impress of an intelligence through which it has passed. It then becomes connected with other facts of one kind or another, and thus originate a certain number of conceptions or theories which make a greater or less number of proselytes. There are certain facts or groups of facts with regard to which, as a result of tradition, the habits of education, or general feebleness of intellect, everyone is agreed; and these are regarded as true and as part of the foundations of science, up till the day when a bolder inquirer thinks of questioning them, banishing them altogether by contradiction, or giving them a new interpretation; thus accepted theories are reversed.

"If truths of the rear-guard are to be treated with caution, how much more so those of the advance-guard, which are the result of recent conquests; for these there is no rule or tradition, each one is free to interpret them as he chooses, . . . one does not discuss the facts but their interpretation. From this it results that even a serious discussion between two keen intellects has no chance of reaching a conclusion as long as it remains in the realm of already ascertained facts. It is only of use when it leads the opponents to seek and to discover new ones."

CHAPTER XX

ORIGIN OF WINE-YEAST

EACH controversy led Pasteur to the discovery of new facts. He asked himself whence came the yeasts which he had shown in his preceding studies to be so many and diverse. Outside a medium adapted to their growth they very quickly perish. One can easily understand the perpetuity of the beer-yeast which the brewer grows in his vats by continually renewed generation; but how is one to account for the fermentation which starts spontaneously each year in the wine-growers' barrels? Whence comes the initial germ from one year to another, the old germ having necessarily disappeared? Pasteur has not altogether solved this difficult problem, but he has lifted a corner of the veil. He has shown that as long as the grapes remain green, the fruit and stalks are incapable of setting up fermentation; but after continued attempts, it will one day be found that there are some grapes and pieces of stalk which will cause the sugar-containing fluid into which they have been introduced to ferment, necessary precautions having been taken to prevent the introduction of foreign germs. From now onwards up to the time of vintage, the yeast germs will become more numerous, first on the stalk, which is always more abundantly supplied, then on the fruit and the shoots of the vine. At all times, however, some isolated grapes are met with which continue incapable of setting up fermentation. When the grapes are harvested without their stalks, the germs are found to decrease in number on the stalks and shoots, until when winter comes they are found to have disappeared entirely.

In order to ascertain the exact moment when yeasts made their appearance, Pasteur passed a damp brush over the surface of grape or stalk, and after a time found that the brush had entangled certain brown corpuscles with thick walls, not resembling any known yeast. These corpuscles, sown in small quantities of sugar solution exposed to air, gave birth to numerous cellules easily recognized as yeast; it sufficed to introduce them into a sweet wort to set up a well-defined alcoholic fermentation. Pasteur was able to correct the idea which he had introduced into the science in a form which by no means satisfied him: "the ferment is a living being which springs from a germ carried in the air." Heterogenesists, especially Pouchet, had the same objection ready which they had urged in the discussions on spontaneous generation: if every bubble of air contained a ferment germ, we should be surrounded by a thick fog. The new experiments, showing that the yeast germs are supplied by the fruit and that oxygen only plays a part in giving power and activity to the ferment, explained what are the actual facts. M. Pasteur was anxious to confront his opponents with an incontestable proof. He has described in his *Critical Examination of a Posthumous Work of Claude Bernard*, how he succeeded: "Regardless of expense I ordered in haste a number of glass-houses with the intention of transporting them to the Jura, where I possess a vineyard of some dozens of square metres. There was not a moment to lose, for the following reason.

"I have shown in one chapter of my *Studies on Beer* that yeast germs do not exist in grapes which are still sour, which is the case in the Jura towards the end of July. We are, I said to myself, at a time of year when growth having been delayed as a result of a cold, wet season, the grapes in the canton of Arbois are still in a sour state. By seizing this moment to enclose the vine-stalks almost hermetically under glass, I shall, at the vintage in October, have vine-stalks bearing ripe grapes on which are no yeast germs. These grapes being crushed with the precaution necessary to avoid the introduction of yeast germs, will neither be capable of fermenting nor of being made into wine. I shall give myself the pleasure of taking some of them back to Paris and presenting them to the Academy, and of offering some to those of our colleagues who still cling to their belief in the spontaneous generation of yeast.

"On August 4, 1878, my houses were completed and ready to be set up. This work was finished in a few days.

"During and after the installation of the glass-houses, I carefully tried to make sure that the yeast germs were, as before, absent from the green grapes. The result was as I had foreseen: in a large number of trials I discovered that the sour grapes in the Canton of Arbois, and in particular those on the stalks under the glass-houses, showed no trace of yeast germs at the beginning of August, 1878.

"For fear lest the glass-houses should not be sufficiently closed to protect the grapes from germs, I took the precaution, while leaving some grapes free, of surrounding a certain number on each stalk with cotton which had been heated to about 150° C.

"About October 10th, the grapes in the houses were ripe, one could distinguish the pips through their skins, and to the taste they were as sweet as grapes ripened in the open; only under the cotton, grapes which should have been black were not fully coloured, and the white grapes had not the golden-yellow tint of those exposed to the sun. In spite of this there was, I repeat, nothing to be desired as to ripeness in both.

"On October 20th I made my first experiment on the grapes left free and those covered with cotton, as compared with those in the open air. The result surpassed my expectations, so to speak. The tubes containing grapes from the open air fermented by means of grape-yeast after from thirty-six to forty-eight hours sojourn in an incubator, the temperature of which varied between 25° and 30°; on the other hand not one of the numerous tubes containing grapes covered with cotton underwent fermentation by alcoholic yeast, and—a remarkable fact—it was the same with the uncovered grapes in the glass-houses. It was the experiment already described in my *Studies on Beer*.

"Next day I repeated the experiment, with the same results.

"A second experiment by way of comparison naturally suggested itself to the mind. When the glass-houses were set up, we were at the beginning of the season, when germs are absent from the vine-stock and fruit. At the time of the experiments we were, on the contrary, at the period when germs are present. Presumably then if I plucked some of the grapes covered with cotton in the glass-houses in order, after having removed the cotton, to bring them into contact with vine-stocks which had remained in the open, these grapes, which immediately before could not ferment on being crushed, would ferment under the influence of the germs which they could not fail to acquire in their new position. This was exactly the result I obtained."

Pasteur did not stop short at these immediate results; his penetrating eye perceived consequences far removed from his discoveries.

"Allow me," he says, "to make an experimental digression well worthy of interest. A bunch of ripe grapes, I have said, carries on the outside germs of ferments which make wine in the vats and barrels of the wine-grower, ferments which belong to the *saccharomyces*. For this reason is it not to be expected that at the time of the vintage, rain must collect many spores and scatter them over the soil of the vineyard? Experiment confirms this anticipation. Having deposited small portions of earth from the vineyard in a series of tubes containing grape-wort preserved by previous boiling, I observed the wort in many tubes of each series entering into alcoholic fermentation. Without injuring the success of the experiment, portions of soil could be taken from a depth in the ground of from ten to fifteen centimetres. What is more usual still in experiments of this sort is an alcoholic fermentation produced by yeast of the species *mucor*—so numerous in the soil are the spores of these minute plants.

"I had the curiosity to compare, with regard to the presence of wine-yeast spores and the spores of *mucor*, the soil of the vineyard with that covered by my glass-houses. With the earth from the houses I never found alcoholic fermentation due to wine-yeast produced in my tubes, although the experiment was frequently performed; on the other hand fermentation by *mucor*-yeast frequently occurred.

"What reflexions are born of these results, and how can one avoid the observation that the further one penetrates into the experimental study of germs, the more one meets with unexpected enlightenment and with correct ideas as to the causation of disease by contagion. Is it not well worth attention, that in the Arbois vineyard (and this would be true of two millions of acres of vineyards in every country in the world), at the time when I made the experiments just described, there was not, so to speak, one particle of earth which was not capable of setting up fermentation due to wine-yeast; and that, on the contrary, the earth in the glass-houses I have described was powerless to produce this result; and why, because at a particular moment I covered the ground with a few panes of glass, should the death, if I may so call it, of a single grape thrown down in any vineyard whatever, have infallibly made the introduction of the parasitic *saccharomyces* of which I am speaking, possible; a death of this nature was impossible in the little plots of ground covered by my glass-houses. These few cubic metres of air, these few square metres of soil surface, were there in the midst of a universal contagion, and were not for many months in any danger from it. But in the case of disease and death due to the parasites of the *mucor*, of what use had been the protection of glass? None at all. The parasites of *saccharomyces* coming from outside at a certain time of the year, a timely protection can keep them off, in the same way in which Europe is preserved from cholera and plague by means of quarantine. The *mucor* parasites, on the other hand, existing permanently all the year round in the earth of our fields and vineyards, are in consequence present under the glass-house at the time of its erection, in a manner resembling in some respects that of our common contagious diseases, against which quarantine, which keeps out plague, cholera and yellow fever, is obviously powerless.

"Is it not permissible to believe on analogy that a day will come when simple preventive measures will check the scourges which suddenly attack and destroy whole populations, such as that terrible malady yellow-fever, which has recently invaded Senegal, or the perhaps even more horrible bubonic-plague which has ravaged the banks of the Volga ?"

The day thus foretold by Pasteur has come ; preventive measures inspired by his work have been taken, and this has been an inestimable benefit to mankind.

CHAPTER XXI

CONTAGION—THE ANTISEPTIC SYSTEM

In 1873 Pasteur had been elected, by a majority vote, Member of the Academy of Medicine in the section of Free Associates. He was neither a doctor nor a veterinary-surgeon, but many of his new colleagues appreciated the importance of his work, and the benefits which medical science would derive from it. Others, on the contrary, viewed with disgust this intrusion of a mere chemist into a department, theirs by tradition, from which they wished to exclude what they contemptuously called *laboratory sciences.* Reports of the experiments of Villemin, Professor at Val de Grâce, which showed tuberculosis to be infectious and inoculable, had been recently received. Pidoux, one of the academicians of highest repute, had solemnly declared that this disease is "one and multiple at the same time," producing the same final result, the microbiotic destruction of an organ by a multitude of ways which the hygienist and the doctor ought to endeavour to close. With such phrases was reply made to experimental facts; it was triumph in a warfare of words only.

Pasteur had been occupying himself for a long time with the application of his discoveries to human pathology. At the time when he entered the Academy of Medicine, ideas about infection were very confused. When any epidemic broke out, its spread was explained with big words of vague significance, such as miasma, medical constitution, epidemic spirit, the *quid divinum* inexplicable and not to be discovered. It was not that the idea of contact, and even living contact, *contagium vivum* or *animatum,* had not been suggested, it is found clearly expressed in old Latin authors. Since diseases have been talked about, all sorts of pronouncements have been made. Towards 1840, Hameau in France and Henle in Germany, had compared the evolution of a disease to that of a living being; and these doctrines, otherwise very different from one another, had both been without success because they were purely mental conceptions, philosophic speculations, which rested only upon observations of disease interpreted in a certain way, which anyone else was free to interpret differently.

It was well known that certain diseases of mucous membrances like *thrush*, or of the skin like *scabies*, could be set up by vegetable or animal parasites; but what relation was there between these superficial external occurrences and infectious diseases which affected the whole body and where nothing external was apparent? Pidoux proclaimed the dogma of *spontaneous morbidity*: "The nature of the disease is to be made in us, of us and by us."

Microscopic study of diseased tissues had led to the conception that pathological conditions are comparable to some physiological ones produced abnormally in regard to the place and time of their production. It was *heterotopy* or *heterochrony*, two hypotheses which again had no reality beyond that of being expressed in Greek words. People were unwilling to admit that living organisms could, when they succeeded in entering the body, bring about specific changes characteristic of a disease. That, they said, would be going back to the ancient and justly condemned idea of a *vital force*. Physiology and pathology were governed by forces of the physico-chemical order.

Surgeons, however, recorded with profound discouragement, the results of operations performed under the most favourable conditions. In 1876 one of them, by no means the least skilful, seeing almost all those he operated on in hospital die, declared that he never wished to touch a knife again. Another advised looking at the deadly knife ten times before taking it up, "for," said he, "if we decide on an operation, we often sign a death-warrant." It was a time when purulent infection, *pyœmia,* reigned. A wretched man being taken to hospital after an accident, incurred when in perfect health, had an amputation performed. After a short interval fever suddenly flared up, his face became livid; all the students and nurses knew that this cadaverous visage signified condemnation to death without appeal.

Surgery had not always been so murderous. The use of dressings as prescribed by Hippocrates of warm water, wine, and vinegar, had been very successful. In 1868, at the Cochin hospital, Leon Le Fort used water containing alcohol, and took care to perform all his operations under conditions of the greatest cleanliness; while his colleagues lost one amputation case in two, he never lost more than one in four.

In 1871, Alphonse Guérin asked himself whether the cause of purulent infection might not be "due to the germs and ferments which Pasteur had discovered in the air. Searching in my despair," said he, "for some means of preventing this terrible complication of wounds, I had the idea that the miasmas, the existence of which I had been obliged to admit because I could not explain the production of purulent infection otherwise, and which were known to me owing to their pernicious influence, might be of the nature of those living corpuscles which Pasteur had seen in the air; from that moment the history of miasmic poisoning was illuminated for me with a new light. If, said I then, miasmas are ferments, I can protect the wounded against their malignant influence by filtering the air as Pasteur has done. I therefore devised cotton-wool dressings and had the satisfaction of seeing my predictions verified." After having washed the wound with carbolized water, or water containing camphorated alcohol, Alphonse Guérin applied to the amputated limb layers of cotton-wool so numerous that after firm compression with many turns of the bandage, the diameter of the dressing was still two or three times greater than that of the limb so dressed. This dressing was left in position for a long time, up to twenty days, and when it was removed, the wound was sometimes found to be half healed. In this way Alphonse Guérin succeeded in saving more than half the cases operated on, which was in those days considered a magnificent achievement.

In the month of February, 1874, Pasteur read with emotion a letter addressed to him from Edinburgh:

"My dear Sir,

Will you permit me to offer you a pamphlet which I am sending by the same post as this, and which gives an account of some researches on a subject round which you have shed so much light: the theory of germs and fermentation. I like to think that you will read with some interest what I have written about an organism which you were the first to study in your *Memorandum on the Fermentation called Lactic.* I do not know whether you have ever come across the *Annals of British Surgery.* If you happen to have read them, you will from time to time have noticed reports of the antiseptic system which for nine years I have been trying to perfect.

"Allow me to take this opportunity of thanking you most heartily for having shown me, by your brilliant investigations, the truth of the germ theory of putrefaction, and for having thus acquainted me with the one principle which can lead the antiseptic system to final success.

"If you should ever come to Edinburgh, you would, I believe, feel rewarded by seeing in our Hospital how greatly the human race has benefited by your work. Need I add that it would give me the greatest satisfaction to show you here what surgery owes to you.

"Excuse the liberty, inspired by our common love of science, which I am taking, and believe me, with profound respect,

"Yours very sincerely,
"Joseph Lister."

The antiseptic system, which justly bears the name of *Lister's Method,* consists in disinfecting everything which can come in contact with the wound, including the hands of the surgeon and his assistants, with a solution of carbolic acid. During the operation a spray plays over the field of operation like a cloud of carbolic vapour ; and the dressings are impregnated with carbolic acid.

In 1869, a house-surgeon in one of the Paris hospitals, Just Lucas-Championnière, had demonstrated the wonderful success of this method. Lister saved thirty-four amputations out of forty. No one paid any attention to the article which the young house-surgeon published in the *Journal of Practical Medicine and Surgery*, nor to a lecture delivered by Lister in 1870 on the results given by antisepsis. The French surgeons, to whom science owed so much progress, showed themselves difficult to convince of something which was against all their habits and which contradicted the accepted theory. Jokes were made about the minute detail of the Lister technique and the fog which enveloped the operator ; but some, better advised, endeavoured to apply the method in every detail, and were not long in recognizing its great value.

CHAPTER XXII

CONTROVERSIES AT THE ACADEMY OF MEDICINE — SPONTANEOUS GENERATION — FERMENTATION—PUTREFACTION

THE work of Pasteur was misunderstood and little appreciated by some of his new colleagues at the Academy of Medicine. He had to put up with much contradiction, which he was not always inclined to submit to with patience, especially when he saw purely theoretical objections made on matters which he had long studied. He replied to M. Poggiale, who regarded the question of spontaneous generation as unsolved and almost insoluble, thus :

" You say that in the present state of science it is wiser to hold no opinion. Very well ! I have one myself, not from sentiment but from conviction, because I have earned the right to have one by twenty years of hard work, and everyone with an impartial mind would be wise to share it.

" My opinion, better still my conviction, is that in the present state of science, as you rightly say, spontaneous generation is a chimera, and you cannot contradict me, because my experiments are sound and all prove that spontaneous generation is a chimera.

" What, then, is your verdict on my experiments ? Do you deny that I have a hundred times put organic matter in contact with pure air under the best conditions for the spontaneous production of life ? Do you deny that I have dealt with that organic matter which is in everybody's opinion most favourable to spontaneous birth, such as blood, wine, and grape-juice ? How is it that you cannot see the essential difference between me and my opponents? Apart from the fact that, proof in hand, I have contradicted every one of their assertions while they have never dared seriously to contradict one of mine, every source of error supports the opinion of those who hold that putrescible matters contain their ferment in themselves. I who uphold that there are no spontaneous fermentations, succeed in avoiding every source of error and all disturbing influences. I can only maintain my results by means of absolutely irreproachable experiments; their opinions, on the other hand, gain from every inconclusive experiment, and only thus do they find support.

"To sum up, what are you, declared partisans of heterogenesis or complaisant and thoughtless upholders of this doctrine, driving at? Are you going to combat my assertions? Do you wish to attack my experiments? Prove them inaccurate, instead of constantly making new ones, which are merely variations of mine, and into which you introduce errors which must afterwards be pointed out to you."

It was said that Pasteur was far from having cleared up all obscurities in the question of fermentations, and he answered:

"What then is your idea of progress in science? Science takes one step, then another, then stops and hesitates before taking a third. Does the fact that this last step is impossible, abolish the progress made by the first two?

"A mother takes her infant child, and putting it on the ground says: 'Walk!' The child (and are we not all children before the mysteries of nature?) takes one step, then a second, then stops and totters. Would you come and say to him: 'Ah! you have taken two steps, but you hesitate over the third; your previous efforts are null and void; you will never walk?'

"You wish to upset what you call my theory, in order to defend another. Very well, let me tell you the signs by which a theory may be recognized as true.

"The characteristic of erroneous theories is that they can never produce new facts, and every time that a fact of this kind is discovered, these theories are obliged, in order to account for it, to graft a new hypothesis on to the old one.

"The characteristic of true theories, is, on the contrary, to be the expression of actual facts, to be ruled and dominated by them, to be able to foretell new facts with certainty because they are naturally linked to the first; in a word, the characteristic of these theories is their fertility."

Pasteur had demonstrated by many examples and important applications in the field of industry that his theories were fertile.

Bouillaud, one of the oldest and most illustrious members of the Academy of Medicine, asked, possibly with a secret desire of embarrassing Pasteur: What then are the ferments of ferments? The answer, which was given at the Meeting of March 9, 1875, is worth recording:

"In a more general way perhaps the question may be put thus. How can ferments, which are living things, and contain substances of the same nature as other living beings, be decomposed as the result of a decomposition which they themselves have initiated? How can they be destroyed and disappear, or at least be reduced to their germs which alone are eternal as far as life can be eternal on the surface of the earth?"

One cannot embrace in the infinite variety of their details all the ways in which after death organic matter returns to the atmosphere or the soil; but nature accomplishes these transformations according to a few general and well-determined laws. Pasteur contented himself with studying these transformations in one example only, that of the grape and added: *ab uno disce omnes.*

He imagines "that all the grapes in a vineyard have been harvested and put in a great mass into an immense tank. The weight of the piled-up bunches begins by separating the grapes from one another, bursts them, and allows their contents to escape in the form of a sweet fluid. By a fortunate chance it happens that at the time when the grapes are ripe, their surface and that of their stalks is covered here and there, in the form of dust, by vast numbers of the germs of a small cellular plant. This has the property, when once it has commenced germinating under the influence of a very small supply of air, of multiplying itself indefinitely in the total absence of free oxygen, and of provoking, coincidently with its life, the decomposition of sugar into carbonic acid gas, which is given off, and into alcohol, which remains in solution in the liquid mass.

"In the grape-wort, the matter of next importance after water is the sugar; of this there is 20 to 25 or more per cent. The decomposition we have just described as accomplished by the ferment, eliminates in the state of carbonic acid gas more than 50 per cent. of the saccharine material. There is therefore a considerable part of the organic matter of the grape which, by the life of a ferment, is returned to the atmosphere in the form of carbonic acid gas.

"This strange phenomenon, which has appealed to the imagination of man since the world began, is accompanied while taking place by intense heat and by the bubbling of the whole mass, but in proportion to the gradual disappearance of the sugar, the heat and movement gradually subside."

The immense vat is now full of wine. Soon there appears upon the surface of the liquid a thin film formed of the mycoderm which will convert the wine into vinegar, a change which will produce no alteration in its volume, and finally the vinegar will be reduced to carbonic acid and water, which will cause a considerable diminution of the total bulk. The mass is then a mere watery solution of small quantities of mineral and organic matters, and at the bottom lies a deposit, formed at first of grape-skins and stalks, later of the yeast of wine and vinegar which have ceased to act and to live.

This liquid has lost all acidity; the germs which float in the air bring it new life; a scum, greasy and mucilaginous in appearance, forms on its surface; the whole mass becomes turbid, and a foul odour is given off which tells of putrefaction. Part of the sulphur, phosphorous and sulphates of ammonia, phosphates and nitrogenous matters which form the deposit, return to the atmosphere in the form of gases. The superficial pellicule contains thousands of millions of aerobic bacteria which oxydize carbonaceous substances in solution, and liberate carbonic acid gas. Below, down to the very bottom layers, the anaerobic vibrions of putrefaction decompose, in the form of sulphuretted hydrogen, ammonia and other evil-smelling gases, a large part of the macerated solids.

When the force of the germs is spent, patches of mould appear on the moist and fatty pellicule which covers the liquid. These new organisms, aerobes and bacteria, will feed on the germs which have preceded them, and on the subjacent matter, by combining oxygen with them and liberating carbonic acid in considerable quantities.

More and more of the dissolved matter and that which is deposited at the bottom of the vat is converted into gases and mineral salts. Constant evaporation set up by the heat of these successive combustions has caused the gradual disappearance of the water contained in the tank; but combustion continues as long as there is any organic matter left.

" When one mould has exhausted itself, if one may say so, by utilizing for its existence that part of the surface or material upon which it has lived, another, to which the first serves as food, replaces it.

" In the end what is left ?

" 1st : Cinders, as if one had set fire to the material, for the slow and successive decompositions produce the effect of fire.

" 2nd : The last germs of the last organisms which have lived on their fellows ; the mineral matter is ready to return to the earth, the organic matter has returned to the atmosphere ; and when all is dried up, the spores of the moulds and the cysts of the infusoria will be carried on the wings of the wind to begin again elsewhere their work of living and of the destruction of life.

" Ferments, and especially aerobic ferments or those which take their place, are therefore the ferments of ferments.

"After the anaerobic ferments have begun the disintegration of the solid matter, aerobic beings intervene and burn it up as surely as does fire; more slowly, it is true, but what matters time in the work of destruction by the life of germs, since in them alone exists the power of perpetuating the life of microscopic beings."

Bouillaud replied by hailing the "triumph" which Pasteur had achieved; and returning to this discussion at one of the following meetings, the old classical scholar, fond of Latin quotations, added: "This exposition of the phenomena and causes of different fermentations, sparkling at the same time with scientific knowledge and poetical fancy, kept us all, every one of us, hanging upon the lips of M. Pasteur:

"*Conticuere omnes intentique ora tenebant.*"

CHAPTER XXIII

PASTEUR REWARDED BY THE STATE

PASTEUR'S health was too uncertain for him to continue to hold his Chair at the Sorbonne. The paralysis of the left side with which he had been stricken was not completely cured; he limped and his left hand had remained disabled and feeble. In 1874, the National Assembly awarded him a pension for life. Paul Bert in proposing the vote said:

"M. Pasteur's discoveries, after shedding new light on the obscure question of fermentation and on the way in which micro-organisms appear, have revolutionized certain branches of industry, agriculture and pathology. One is filled with admiration at the sight of so many different results emerging by the linking together of facts, followed step by step and leaving nothing to hypothesis, from theoretical studies on the way in which tartaric acid deviates polarized light. Never has the famous saying "genius is patience" received such striking confirmation.

"It is this admirable combination of theoretic and practical work which the Government proposes that you should honour with a reward from the Nation. Your committee unanimously approves of the proposal.

"The reward asked for is a life-pension of 12,000 francs; this sum represents very nearly the amount of the salary attached to the Chair at the Sorbonne, which illness compels M. Pasteur to relinquish. It is undoubtedly a very modest one in comparison with the value of the services rendered."

The vote was passed almost unanimously.

Urged by some of his compatriots, Pasteur consented to become a candidate at the elections to the Senate of 1876. He proposed, if elected, to plead before the Upper House the cause of higher education. The electors of the Jura, who numbered six hundred and fifty, gave him sixty-two votes. They allowed themselves to be influenced by Jules Grévy who said, with calm conviction, that the place for men of science is the Institute and not the Senate. Those elected had this advantage over Pasteur, that they did not mortify the electors by any superiority over them.

This year, 1876, had a compensation in store for Pasteur. He took part, as delegate of the French government, in an International Congress on Sericulture, held at Milan, where Italy, Russia and Austria were also officially represented. His pupils, Duclaux, Raulin and Maillot expounded his principles, which met with no opposition. It was at a banquet at the close of the Congress that he pronounced the words so often repeated since: "Science has no country, but the scientist has one."

He wrote on September 17th, to J. B. Dumas, his revered master: "The Congress being over, we are spending a day or two at the country house of M. Susani, in the heart of Brianza. For ten hours a day, since the 4th of July, sixty or seventy women have been here engaged, methodically and under strict supervision, with microscopical examinations. No factory is better organized. Forty thousand moth-specimens are examined each day. The neatness and orderliness are marvellous. All possibility of error is avoided by the institution of two controls. It has given me a pleasure which has, to a great extent, compensated me for the frivolous opposition with which some of my compatriots have pursued me for many years, to see my name written in large characters on the front of this institution; this is a spontaneous act of homage paid by the proprietor to my researches."[1]

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[1] **Quoted by René Vallery-Radot, *op. cit.* p. 363.**

CHAPTER XXIV

ANTHRAX

Except during a few rare periods of absence, Pasteur worked every day in the enlarged laboratory. Duclaux writes that personally " he was indifferent to perfection of technique; complicated apparatus mattered little to him; it was enough for him if he could obtain from it definite and unequivocal answers to his questions. But it is possible to combine accuracy with a simple question or a prompt reply. This is the function of a good technique. That of Pasteur's laboratory had its origin in the ideas and discoveries of the master, but it is only fair to say that in itself it was the creation of the three collaborators, whom it was Pasteur's good fortune to meet at this time, Joubert, Chamberland and Roux."

Raulin, another of his pupils, had while studying according to Pasteur's principles, the common mould *aspergillus niger*, obtained results of great importance, which he incorporated in a pamphlet modestly entitled *Chemical Studies on Vegetation*. After innumerable trials. he had determined the composition of a liquid more suitable than any other to this mould. This fluid, since rightly known as Raulin's Fluid, contains, in more water than is necessary to hold them in solution, ten definite chemical substances. All these substances, to which must be added oxygen from the air, co-operate simultaneously in the development of the plant, for if they are eliminated one by one, or if their proportions are altered, growth is immediately retarded.

In this favourite medium, if kept at a temperature of 35° C., and having the damp air which it requires, the *aspergillus niger* grows with such vigour that it has nothing to fear from any parasite. This, says Raulin, is " because the medium most suited to the development of one form of vegetation, is less suitable to any other form, and if the germs of both kinds are sown in the same medium, the first only will develop, or at least will end by invading the whole medium at the expense of the second." It is not enough to give the plant the foods that suit it best, one must also remove from the nutrient medium all injurious elements; an infinitessimal trace of a silver-salt will stop the development of the *aspergillus niger*; it cannot be cultivated in a silver vessel; " although it is almost impossible to give chemical proof that any part of the material of the vessel has dissolved in the liquid, the plant demonstrates it by dying." (Duclaux).

Pasteur remembered these points, and each time that he encountered a fresh species, he hastened to find out the culture-medium best suited to its requirements.

When he, thus armed, approached the study of the *bacillus anthracis*, he had no difficulty in progressing faster and further than all those who had preceded him.

In 1850, Rayer and Davaine had seen little rods in the blood of sheep which had died of what was then called *sang de rate;* they noted the agglutination of the red and the abundance of the white corpuscles. In 1855, Pollender confirmed this observation, and asked himself whether these little rods, to which neither Rayer nor Devaine has attached any importance, did not constitute the infectious matter. Brauell replied in the negative, because he confused the rods with the ordinary bacteria of putrefaction.

Delafond returned to the previous position, He showed that the rods appear in the blood of animals suffering from anthrax during life; the bacteria of putrefaction only show themselves after death, and in proportion as they develop the rods disappear. He proved that the rods are of vegetable nature, since they are seen to grow in blood exposed to free air in a suitable temperature. He even tried to continue the growth of the vegetation as far as the production of spores, but in this he was not successful.

These results did not modify accepted opinion. Anthrax was known to be inoculable and contagious. It was attributed to an invisible virus, like that of small-pox or sheep-scab, living on the life of the animal which carries it and dies of it. How could anybody admit that a microscopic rod, living its own life, could suffice to kill an ox? And this rod did not appear in the blood at the beginning of the disease, but only a few hours before death: How could one suppose it to be the cause of anthrax?

Davaine had read, in 1861, Pasteur's brief communication on butyric fermentation. He saw what great effects this vibrion, which is a rod similar in form to that of anthrax, in spite of its microscopic dimensions, can produce by its fermenting action, and he was not surprised that the anthrax rod, to which he gave the name of *bacteridium*, could kill a horse or an ox.

He proved by numerous experiments that there is no anthrax without bacteridia. Many observers denied this. In particular two professors of Val de Grâce, Leplat and Jaillard, had killed rabbits by inoculating them with anthrax-blood which had been sent to them from Chartres, and had not succeeded in finding bacteridia in the blood. Davaine, after repeating their experiments, replied that in some cases they had failed to recognize the bacteridium, and in other cases the disease they had observed was not anthrax; and in fact, in the latter cases, both the duration of incubation and the lesions discovered at the postmortem had not been the same as in anthrax.

Davaine completed his demonstration by proving that the blood of the animal is only contagious when the bacteridium is present. When, owing to the advance of putrefaction, it has disappeared, the blood is no longer capable of communicating anthrax. Davaine added a very valuable argument to these statements. He filtered some anthrax-blood in such a manner as to retain all the visible bodies, globules and bacteridia, and only to let through the serum and the soluble elements : inoculation with this serum did not produce anthrax.

The bacteridium is therefore proved to be the cause, and the sole cause, of anthrax. It remained to be shown why it develops an epidemic or an endemic character according to time and place. Davaine knew that contagion is no longer possible when once putrefaction has begun in the body of the anthrax-infected animal ; but he observed that blood, dried quickly enough to avoid putrefaction, retained its virulence for a long time. The peasants wished to save at least the skin of the animals they lost, and in removing it spilt a good deal of the blood about. The germs were then carried by flies which had alighted on the dried blood. Davaine proved by admirably conducted experiments, that things could happen thus, and one must admire the wisdom of this doctor, who, dependent entirely on his own resources, and with inadequate means of pursuing his researches, threw so much light on this difficult question.

But how can one explain by Davaine's hypothesis the so called *champs maudits*, the accursed fields of the Bauce, or the *montagnes dangereuses*, the dangerous mountains of Auvergne, where no flock can be pastured without some animals falling victims to anthrax ? Flies are no respecters of fences, and if they were the habitual agents of the infection, one would always find on the spot which they had bitten or stung something analogous to the *malignant pustule* in man, in whom anthrax always begins by injury to mucous membrane or skin. Now it is very rare to see a similar beginning in domestic animals. Is it not natural in these conditions to attribute the danger of the *cursed fields* to some quality peculiar to vegetable growth or soil ?

Koch removed these difficulties to a great extent when he discovered the anthrax spore. In 1869 Pasteur had seen in the vibrion of flachery, bright corpuscles which he called cysts, and he had attributed the fact that this disease of the silk-worm was endemic to the resistance of these cysts, which was much greater than that of the vibrion where they appeared. Koch gave an analogous demonstration with regard to the anthrax bacteridium.

He was not content, like Delafond or Davaine, with studying the blood. He took a minute fragment of spleen from a mouse which had just died of anthrax, and introduced it into a drop of fresh serum from ox-blood or into a drop of the aqueous humour of the eye, two liquids which form fairly good culture media. On examining under the microscope this drop, spread between a slide and a cover-glass, he saw that only in the middle of the glass, where air did not penetrate, the bacteridia preserved their original appearance and length; but in proportion as they approached the edge, they stretched out more and more until they became a tangle of flexible filaments. Those of these filaments which are in the immediate neighbourhood of the outside air contain typical spores, arranged in their envelope, according to the picturesque phrase of Tyndall, like peas in a pod. The envelope is re-absorbed, and the liberated spores spread themselves about the liquid like specks of dust. But these specks are really seeds; sowed in a fresh drop of serum, they produce bacteridia identical in form with those from which they come and like them capable of causing death by anthrax.

Koch showed that two conditions are necessary for the production of spores: a suitable temperature and oxygen. At 30° C. spores form in thirty hours, at 35° in twenty hours. On the other hand, if one protects the anthrax blood from air, while preventing it from putrefying, after a time it will lose its virulence. It also loses it by putrefaction, when this putrefaction develops rapidly enough to absorb the oxygen before the spores have time to form; but if time for this is allowed, the spores can co-exist with the bacteria of putrefaction. Thus the contradictory results obtained by different observers are explained. The resistance of the spore also explains the persistance of the disease in a place where a first case has appeared.

Finally Koch succeeded in giving anthrax to small animals by mixing bacteridia or spores with their food.

The problem might have appeared quite solved, when Paul Bert suddenly affirmed, in 1877, that he could kill the bacteridia in the blood by means of compressed oxygen, and that the blood thus treated remained capable of transmitting the disease without its being possible to find the bacteridium in the inoculated animals.

That anthrax was an inoculable and contagious disease was a fact beyond dispute ; but, in the inoculated matter, what was the real cause of the disease ? The visible parasite, the bacteridium ? Or, as in small-pox, and in sheep-scab, something invisible called virus ?

Chaveau had distinguished virulent diseases from contagious non-parasitic diseases. Nothing absolutely proved that anthrax was not one of these. In inoculating anthrax-blood, it is not only the bacteridium which one introduces into the organism, but also white and red corpuscles, and the serum which carries them, with all the other elements which this contains, among which may be a virus. Chaveau had demonstrated that virus consists of solid and defined corpuscles which are indistinguishable among the more or less amorphous granulations of organic fluids. They only develop in a suitable organism ; or, it was thought, that they form themselves at the expense of the living matter from which they proceed, by means of chemical modification. They are retained by a filter with fairly fine pores : the experiments of filtration by which Davaine thought he had demonstrated the exclusive action of the bacteridium are therefore not conclusive.

The successive cultures of Koch are more so. He sowed a particle of anthrax-infected spleen in a drop of serum. This drop served to sow a second, which served for a third, and so on up to an eighth culture. The virus, if virus there were, should then be very much diluted, and nevertheless it was possible to inoculate anthrax with the eighth drop. But Chaveau had shown that some kinds of virus remain active in spite of considerable dilution, that is to say, up to a hundred and fiftieth part in vaccine, and a five hundredth in glanders, which was then considered a virulent disease. It followed that the supporters of parasite and those of virus continued to dispute as to the origin of anthrax.

Besides this, since Pasteur's discoveries, the question of microbes in connection with disease, had incited more and more numerous experiments. A great variety of microbes was found in pus from the same source. Some which appeared exactly the same were found in quite different diseases. There was great confusion. Pasteur wished to put an end to it.

It was in 1877 that Pasteur, with the collaboration of Joubert, made his first experiments on anthrax. His first step was to find a suitable culture medium, and it appeared that urine, rendered neutral or slightly alkaline, fulfilled the necessary conditions. He therefore introduced a drop of anthrax blood into a capsule of urine, and the bacteridia multiplied there abundantly in the form of the long-tangled filaments described by Koch. He put a drop charged with bacteridia into a second capsule, and a drop from this into a third; this was done forty times, a hundred times, and could have continued indefinitely; in every case one drop of the last culture gave anthrax as surely as the original drop of blood.

Taking the amount of urine used in each culture as fifty square centimetres, the original drop of blood is diluted to a thousandth in the first capsule, and to a millionth in the second, and one must add three noughts to this figure to measure the degree of dilution in each succeeding culture; at the hundredth this degree is represented by the unit followed by three hundred noughts, a number so formidable that we can form no conception of it: it is enough to reflect that after the first proceedings the original drop is as it were lost in an ocean, and that at the ninth the degree of dilution, represented by the unit followed by twenty-seven noughts, is the equivalent of what would be obtained if one put the original drop into a volume of water equal to the total volume of the earth. All that this drop brought with it, apart from the bacteridia which multiply in the culture, is diluted to complete exhaustion in these enormous quantities. Pasteur could assert, and this time without possibility of contradiction, that the bacteridium is the sole cause of anthrax.

He adds: It is the bacteridium itself and not a soluble poison which it carries, because it is enough to filter the culture fluid through a porous substance to render it innocuous. One obtains the same result by decanting. In a place like the cellars of the Observatory, where the temperature is invariable and not high, all the bacteridia form a deposit. The upper layers of the fluid can then be inoculated in great quantities into animals without making them diseased, whereas the inoculation of the smallest particle of the deposit kills them. Anthrax is purely "the disease of the bacteridium, as trichinosis is the disease of the trichina, and scabies the disease of the acarus."

From this time some of the obscurities which this disease presented were cleared up. Nothing is known of virus apart from the effect it produces on the organism which is attacked. But a parasite can be cultivated separately, one can study its properties in a culture medium, and that greatly facilitates the study of its action upon the living animal.

Since the time of Koch it is known that the bacteridium cannot exist without oxygen: when it invades the blood it absorbs the oxygen from the corpuscles, hence the blackish colour of the blood and viscera, which sufficiently resembles the colour of coal to have occasioned the name *charbon* given to this disease in France.

Rayer and Davaine had pointed out, as early as 1850, the agglutinated state of the red corpuscles. Pasteur showed that filtered anthrax serum agglutinated corpuscles taken from the veins of a completely healthy animal; this action is therefore due, not to the bacteridium itself, but to a secretion which it has produced in the serum.

Blood taken from a vein and collected in a capsule is an excellent culture medium; in a few hours the bacteridia sown there will invade it completely. On the contrary, blood contained in the vessels is one of the worst culture mediums. Pasteur explains this apparent contradiction: "With inferior beings, even more than with the higher species of animals and vegetables, life prevents life. . . . It must be remembered that living blood in full circulation is filled with an infinite number of corpuscles which require, in order to live and to fulfil their physiological functions, free oxygen gas: one may say the blood corpuscles are aerobes *par excellence*. As soon then as the anthrax bacteridium penetrates into normal blood, it encounters a vast number of organized individuals ready for what is sometimes called, in imaginative language, the struggle for existence; ready, in other words, to seize for themselves the oxygen necessary to the life of the bacteridium."

Also the bacteridium injected into the jugular vein of a guinea-pig in perfect health, develops with difficulty, and death ensues no sooner through a hypodermic injection. If the injection is made in the jugular vein of a hen, not only does the bacteridium not develop, but it quickly disappears. Hens, for a reason with which Pasteur was not yet acquainted, are immune to anthrax.

All aerobic microbes can play the same part as blood corpuscles: they prevent the development of the bacteridium in neutral urine, because they take from it the oxygen which it requires, and they act in the same way in the body of an animal. "One can introduce a profusion of anthrax bacteridia into this animal without its contracting anthrax. It is only necessary to add some common bacteria to the inoculation fluid." Pasteur thus gives the first example of what was to be called *bacterio-therapathy*.

CHAPTER XXV

THE VIBRION-SEPTIQUE—THE GERM THEORY

Davaine had replied to Leplat and Jaillard, who killed an animal by inoculating it with anthrax-infected blood and found no bacteria: "It is not anthrax which you have inoculated." He supported this assertion on clinical grounds and on the postmortem findings, but his arguments though weighty were not convincing. Pasteur wished to repeat the experiment. Leplat and Jaillard were in the habit of receiving anthrax-blood from a knacker's yard near Chartres. Pasteur went himself to this yard. He found there the carcasses of three animals which had died of anthrax: a sheep, which had been dead for sixteen hours, a horse and a cow, the former had been dead twenty-four hours, the latter more than two days. Some guinea-pigs were immediately inoculated; all died. Those inoculated with the sheep's blood showed only bacteridia. In the others were found, in the tissues and peritoneal fluid, innumerable bacilli, which were also present in the blood, but not easily discovered, being few and in the form of long filaments hidden among the corpuscles. Davaine had not perceived them. Pasteur gave this new bacillus the name of vibrion-septique. His investigation, immediately begun, revealed to him a number of important facts.

The vibrion-septique is a common bacillus. It is often found by the thousand in the alimentary canal, the walls of which act, during life, as an impermeable barrier; but after death the impermeability disappears, and the vibrion penetrates into the blood, which quickly acquires great virulence. A Parisian veterinary-surgeon, Signol, had recognized this virulence when he inoculated blood, taken sixteen hours after death, from a healthy animal killed by asphyxiation. Pasteur showed him the vibrion, difficult to see for the first time; it was long and transparent, "creeping about in a sinuous manner, pushing its way between the blood corpuscles as a snake glides between grasses in a thicket."

The disease produced by the vibrion-septique, septicæmia as it was called later, develops more rapidly than that of anthrax. When the two diseases are inoculated at the same time, the animal dies of septicæmia before anthrax has had time to develop. This explains the experiment of Leplat and Jaillard. The anthrax-blood which they had received in Paris, coming from Chartres, had been inoculated more than twenty-four hours after death, and was already septic.

The new vibrion is anaerobic and can only be cultivated when protected from air. Pasteur had established long before that this characteristic is associated with fermenting power, and the vibrion-septique does actually ferment the culture medium, on the surface of which bubbles of different gases are seen to be given off, notably those of sulphuretted hydrogen, which is easily recognizable by its unpleasant smell. An analogous fermentation is observed in an animal attacked by septicæmia. Some hours before death it already exhales a characteristic odour, and after death the body swells, a fatty liquid is seen issuing from the nostrils, and at the post-mortem quantities of fluid mixed with bubbles of gas run out of all incisions.

Pasteur was not long in communicating to the Academy the results of his discovery. It was on April 30, 1878, in a celebrated lecture that, in his own name and that of his collaborators Joubert and Chamberland, he elaborated his *Germ Theory, and its application to Medicine and Surgery.*

Since the new germ is anaerobic:

"By exposing a fluid charged with the vibrion-septique to contact with pure air we ought to kill the vibrions and abolish all virulence. This is what happens. Place a few drops of the septic fluid, spread out very thin, in a tube lying horizontally, and in less than half a day the liquid will have become absolutely harmless, even when, to begin with, it was so virulent that a very small fraction of a drop would cause death on inoculation.

"Furthermore, all the vibrions which were present in the liquid in profusion, in the form of active filaments, have been destroyed and have disappeared. One only finds, after the action of the air, fine amorphous granules, useless for cultivation as well as for the communication of any disease. One may say that the air has consumed the vibrions.

If it is an alarming thought that life may be at the mercy of the multiplication of these infinitely small beings, it is consoling also to hope that science will not remain for ever powerless before such enemies, when one sees it teaching us, at the very beginning of our study of them, such facts as this, that simple contact with air sometimes suffices to destroy them."

This inability to live in contact with air must have brought about the disappearance of the vibrion-septique did it not produce spores not affected by the action of oxygen, and resistant to temperatures of 95° C.

Pasteur had seen the vibrions disappear from septic fluid exposed to air in a thin layer; but the effect is quite different if one allows the fluid greater depth, which must not however exceed that of a centimetre. Then in the upper layers the oxygen is absorbed and the vibrion dies. In the lower layers, "the vibrions protected from the action of the oxygen by the others which have perished above them, continue to multiply by division, and gradually absorbing the rest of the body of the filiform vibrion, pass into the form of spores. Then, instead of moving filaments of all linear dimensions, whose length often exceeds that of the field of the microscope, one only sees a powder of brilliant dots isolated and enveloped in a scarcely visible amorphous matrix. Thus is formed—living the latent life of germs—thus, I say, is formed the septic dust, and we now possess a knowledge of that which only just before seemed so mysterious; we can understand how putrescible materials receive the seed from atmospheric dust; we can understand the constant presence of diseases of putrefaction on the surface of the earth."

It is important to know whether, apart from the vibrion-septique, there is any virulence independent of it, which exists in solid or liquid matter; whether, in fact, the vibrion-septique is only "an epiphenomenon of the disease of which it is the necessary associate." Now one can see septic fluid, taken when the vibrions are not yet changed into spores, lose all virulence by simple contact with air; and, on the other hand, preserve this virulence, although exposed to air, as a result of simply having been in a medium of a certain depth for some hours. In the first case the medium is incapable of renewing its virulence on cultivation; in the second it retains, and can propagate anew, this virulence, even after having been exposed to air. It cannot therefore be upheld that, apart from the vibrion and its spore, it has any special virulence.

These experiments removed the objection raised by Paul Bert to Koch's statements. Like Leplat and Jaillard, Paul Bert had received from Chartres anthrax-blood containing the vibrion-septique and its spores; on submitting the blood to the action of oxygen, he killed the vibrion, but the spores remaining untouched, produced septicæmia on inoculation.

Pasteur gave a direct demonstration of the possibility of the co-existence of the bacteridium and the vibrion-septique in anthrax-blood. He took blood from an animal which had died of anthrax twenty-four hours before, and obtained either the bacteridium alone or the vibrion, according to whether the culture was made in contact with air or not.

The vibrion-septique, a common germ, flourishes in the intestinal canal of all animals. From thence it reaches the soil, where it can almost always be found. Pasteur has shown that by inoculating the washings of almost any soil into a guinea-pig, one can produce septicæmia almost with certainty.

Why then is septicæmia not more common? Because the conditions of the life and development of the vibrion are not always fulfilled.

Pasteur asked himself whether "the spores of the vibrion, although formed in vacuo, or in pure carbonic gas, would not require for renewed life small quantities of oxygen. The physiologist had up till now never known germination to occur out of contact with air. Very well! In spite of this, experiment proves that the germs of the vibrion-septique are absolutely sterile in contact with oxygen, whatever the proportion of this gas; but always provided that there is a certain relation between the number of organisms and the volume of air, because the first germinations, by removing the air, which is dissolved, may protect the remainder, and thus it is that strictly speaking the vibrion-septique can be propagated even in the presence of small quantities of air; this propagation being however quite impossible where air has free access."

Some common bacteria can play a similar protective part, and this is what happens in the intestinal canal where the germs find a medium normally freed from oxygen.

Pasteur, addressing himself to the medical profession, added: "One curious therapeutic observation suggests itself. Let us suppose a wound exposed to air under conditions of sepsis, which may subject the patient to ordinary septicæmic accidents, I mean to say without other complications than would result from the development of the vibrion-septique. Well, theoretically at least, the best means one could adopt to avert death would consist in washing the wound continually with ordinary aerated water, or in allowing air to flow over its surface. The vibrion-septique, as far as division is concerned, would perish in contact with air; as for the spores they would all be sterile. Further, one could allow air to reach the surface of the wound laden with vibrions-septiques and wash it with water holding thousands of millions of these germs in suspension, without producing septicæmia in the patient by these means. If, however, under such conditions, one clot of blood or one fragment of dead flesh is allowed to lodge in a corner of the wound which is protected from the oxygen of the air, and surrounded by carbonic acid gas, if only over quite a small surface, in less than twenty-four hours an infinity of vibrions will be propagated by fission and will be capable in a short time of setting up a mortal septicæmia."

Pasteur also noted the existence of other aerobic and anaerobic germs which are commonly met with in water or air, and which after inoculation do not develop; for some the temperature of the body is too high; for others the tissues into which they penetrate are too much impregnated with oxygen; but if vital resistance be altered, that is to say, if the temperature of the body be lowered or the blood be less rich in oxygen, then one will see germs develop and septicæmia appear.

If one injects a drop of vibrion culture into the muscles of the leg the flesh becomes gangrenous, turns green, and is converted into blood-stained pulp. Germs brought by direct contact are more to be feared than those from the air. Pasteur said to the surgeons: "This water, this sponge, that lint with which you wash and cover the wound, leave on it germs which, you note, are particularly adapted for development in the tissues, and which will infallibly cause in a very short time the death of those operated on, unless the vitality of the tissues prevents the multiplication of the germs; but, alas, how often is the vital resistance powerless; how often does the constitution of the patient, his feebleness, his mental condition, and the bad state of the dressings, oppose only an insufficient barrier to the invasion of these infinitely tiny things with which unknowingly you have covered the wounded part.

"If I had the honour to be a surgeon, convinced as I am of the dangers which micro-organisms scattered over the surface of all objects threaten, especially in hospitals, not only would I use perfectly clean instruments, but after having washed my hands with the greatest care and passed them rapidly through a flame (which is no more unpleasant than what a smoker does when he passes a burning coal from one hand to the other), I would employ only lint, bandages and sponges previously exposed to air raised to a temperature of 110° C. to 120° C. All this is quite practicable. In this way I should have only the germs in the air round the patient's bed to fear; but observation teaches us daily that the number of these germs is, so to speak, insignificant beside those which are scattered in the dust, on the surface of objects, or in even the cleanest ordinary water. Moreover, there would be nothing to interfere with the antiseptic method of dressing, but combined with the precautions I have suggested it could be much simplified. A dilute carbolic acid solution, and one therefore which does no harm to the hands of the operator or his respiration, can be substituted with advantage for a caustic one."

In these suggestions of Pasteur one can foresee the aseptic method; prevention is better, and more certain, than cure; on the day when the surgeon performing an operation on uninfected tissues will touch them only with his hands, or sterilized objects, the use of antiseptics will be no longer necessary.

In this manner Pasteur gave his colleagues of the Academy of Medicine to understand that they bore part of the responsibility for the accidents to which those whom they operated on were victims. He ended thus: " Some weeks ago one of the members of the section of Medicine and Surgery in the Academy of Science, M. Sedillot, after long meditation on the experiences of a brilliant career, had no hesitation in declaring that both the successes and failures of surgery found a rational explanation in the principles upon which the germ theory rests, and that this opened the way to a new surgery already inaugurated by the celebrated English surgeon, Dr. Lister, who was among the first to grasp its possibilities. Without professional experience, but with the conviction of an authorized experimenter, I venture to repeat the words of our eminent confrère."

Sedillot sadly recalled how many wounded he had seen die, during the war of 1870, in his ambulance at Haguenau, whom he might have saved had he known of Pasteur's experiments and of how Lister had applied them. He said to his colleagues of the Academy of

Science: "We shall have assisted at the conception and at the birth of a new surgery, daughter of science and art, which will not be the least of the marvels of our century, and with which the names of Pasteur and Lister will always be gloriously linked."

It was in this communication that Sedillot proposed the name of *microbes* to designate those microscopic beings whose number daily increases.

CHAPTER XXVI

ANTHRAX IN FOWLS

PASTEUR'S statements continued to provoke lively controversy in spite of everything. At the Academy of Science, Colin of Alfort, a great worker, but muddleheaded, restless and suspicious, did not cease repeating that the bacteridium had nothing to do with the virulence of anthrax. Pasteur had said incidentally in his lecture of July 17, 1877, that birds, and particularly hens, are immune to anthrax. Colin, who had a genius for contradiction, hastened to declare that it is quite easy to give anthrax to hens; and this gave rise to an incident which Pasteur took a malicious pleasure in recounting at the Academy of Medicine during the meeting of March 12, 1878.

" As M. Colin had just asked me to be good enough to give him one of my cultures in an absolutely pure state, I wrote to him the next day these few lines :

" ' My dear confrère, I hold at your disposal an absolutely pure culture of bacteridia ; but, as you give anthrax so easily to chickens, I shall be much obliged if, when you come to my laboratory to fech this culture, you will kindly bring me a hen dying of anthrax.'

" At the end of the week I saw M. Colin coming into my laboratory, and even before shaking hands I said to him : ' What about my anthrax hen, haven't you got it ? ' M. Colin answered : ' Rely on me, you shall have it next week.' I went for my holiday. Immediately after my return, at the first meeting of the Academy which I attended, I went up to M. Colin and said : ' And my hen dying of anthrax, where is it ? ' M. Colin replied : ' I have just resumed my experiments on anthrax; in a few days I will bring you an anthrax hen.' Days and weeks passed, not without fresh requests from me and renewed promises from M. Colin. One day, about two months ago, M. Colin confessed to me that he had been mistaken, and that he could not give anthrax to fowls. 'Very well, my dear confrère,' I said, 'I will show you that it is possible, and it is I who will bring to you at Alfort one of these days a hen dying of anthrax.'"

It was not at Alfort that Pasteur presented this hen to his opponent, but at a full meeting of the Academy of Medicine, March 19, 1878.

He had, in the course of his researches, met with a vibrion which could not live at the body temperature of animals. This gave rise to numerous experiments on the limits of heat resistance in microscopic organisms. He discovered in this way that in certain culture media the anthrax bacteridium does not develop, or only does so with great difficulty, at temperatures of 43° C. or 44° C. Could not this be the explanation of the well-known though very mysterious fact that certain animals are immune to anthrax? Fowls have a normal temperature of 42° C., and as "life prevents life," the bacteridia must have much greater difficulty in developing in a living medium than in culture broth. Pasteur and his collaborators, Joubert and Chamberland, found that by putting the fowls into water at 25° C., in such a way that the lower parts of their bodies were covered, it is easy to lower their temperatures to 37° or 38°, which is the temperature of animals susceptible to anthrax, and, as they foresaw, from this time the immunity of fowls no longer exists.

Consequently Pasteur, on March 19, 1878, placed a cage containing three fowls on the desk of the Academy: one, which was white, was dead; two others, one black and one grey, were alive. He told their story.

The white and grey fowls had been placed at the same time in the same bath at 25° C. The grey fowl, intended simply to serve as a control to prove that the bath in itself was harmless, was left untreated; its fellow had been inoculated with five drops of an anthrax culture. The black one had not been put into a bath, but had been inoculated with ten drops of culture, twice the dose of the dead hen ; as a result both the black and the grey were in perfect health.

A fourth experiment made in the laboratory completed these results. A hen immersed and inoculated was kept in the bath until anthrax disease showed itself by the usual symptoms. It was then taken out of the water, wrapped in cotton-wool, and warmed in an incubator. This was sufficient to cure it.

CHAPTER XXVII

FURUNCULOSIS—OSTEOMYELITIS—PUERPERAL INFECTION

PASTEUR was more and more drawn by his researches to deal with the facts of human pathology. "In May, 1879," he says, "one of the workers in my laboratory had numerous boils, developing in rapid succession, sometimes on one part of his body, sometimes on another. I asked myself whether the pus from the boils would not contain one of these micro-organisms, the presence, development and accidental conveyance of which, here and there in the system, after entrance had been gained, could provoke a local inflammation and the formation of pus, and so explain the recurrence of the evil during a variable period of time." A drop of pus from one of these boils, taken with proper precautions and cultivated in broth, did actually show the presence of a microbe, presenting a mass of rounded granules, comparable to bunches of grapes, whence the name *staphylo-coccus* which it received. The same microbe was observed in boils on several other people.

Some time afterwards Pasteur found this microbe in the pus from a case of osteomyelitis which a surgeon had asked him to examine, and had no hesitation in saying: "In this case at least osteomyelitis was a boil of the bone marrow." This dictum which identifies a serious disease of the bone marrow with a common disease of the skin, gave offence; but it nevertheless expresses the truth. Rodet has shown that in young animals, still growing and therefore liable to osteomyelitis, one can set up suppuration in bone by injecting some drops of a staphylo-coccus culture.

These researches obliged Pasteur to pay frequent visits to the hospitals. Dr. Émile Roux, one of his favourite pupils, has preserved his recollections of them in his very interesting note on *The Medical Work of Pasteur*.

"Chamberland and I assisted him in his studies. It was to the Cochin or to the Maternity Hospital that we most often went, carrying our culture tubes and sterilized pipettes into the wards or the operating theatre. It is difficult to realize the repulsion that Pasteur had to overcome in order to visit the sick and to assist at post-mortems. His was such an extreme sensibility that he suffered both physically and mentally in witnessing the pain of others; the cut of the bistoury which opened an abscess made him shudder as if he had himself felt it. The sight of a corpse and the melancholy work of autopsy revolted him. How often did we see him obliged to leave the hospital theatre, overcome! But his love of science and thirst for truth were too strong,—he came back next day."

Pasteur followed with keen interest the discussion on puerperal septicæmia, which had begun at the Academy of Medicine.

Child-birth is a physiological function which ought normally to take place without injury to the mother, and this is generally the case in the country, where in spite of the inadequate care which many women receive, accidents are rare. The state of affairs in large towns was, however, very different. About 1850 a mortality was recorded in Paris of one woman in every two hundred newly confined, and the number was ten times larger in hospitals, although attended there by doctors of the highest standing; and sometimes terrible epidemics occurred which made it necessary to close the maternity wards. At the Paris Maternity Hospital one case was lost out of every four confinements.

The same causes were cited to explain these disasters as were invariably put forward in all epidemics: over-crowding, infection and miasmas. Pasteur could not be satisfied with such trivialities, and said so plainly to his colleagues of the Academy.

"In my opinion no such thing exists as a healthy or an epidemic state. The facts hidden beneath the expressions *infected countries*, *epidemic neighbourhoods*, correspond to a varying abundance of germs, and to hygienic conditions, constitutional or otherwise, which are favourable or not to their development." These expressions were constantly used with regard to pebrine, and in this connection Pasteur added: "I could give you absolute proof that when one has once obtained silk-worm eggs entirely free from disease, it is easy, in the midst of so-called epidemic conditions in an infected country, either to keep the strain raised from this seed healthy or to allow it to become infected. If, for example, one raised this stock under the same roof as infected stock, although on separate and distinct trays, infection shows itself: all the chrysalids and all the moths become diseased and produce eggs doomed to perish. The healthy seed, on the contrary, remains healthy, or only produces a few diseased moths, if one raises it apart and does not allow those who come and go in the *magnanerie* to bring the infection with them by more or less frequent visits. I venture to advise all young doctors to read very carefully my *Studies* on silk-worms; they will find there the first account of a disease, at the same time hereditary and contagious, followed out not only as regards its characteristics and the lesions it causes, but also in the properties and development of living microscopic contagion."

Roux has told about the result of his master's researches: "In puerperal infections the pus from the uterus, that in the peritoneum, and the blood corpuscles in the veins, contain a microbe which has the appearance of strings of beads. This appearance is particularly noticeable in cultures. Pasteur had no hesitation in declaring this microscopic organism to be the commonest cause of infection in women after delivery.

"One day, during a discussion on puerperal fever, one of those of his colleagues whose utterances received greatest attention was discoursing eloquently on the causes of epidemics in maternity hospitals. Pasteur interrupted him from his seat: 'What causes epidemics is nothing of the sort; it is the doctor and his assistants who carry microbes from a sick woman to a healthy one!' And when the speaker answered that he feared that this microbe would never be discovered, Pasteur rushed up to the black-board, and drew the organism in chains, saying: 'Look! that is what it is like!' His conviction was so strong that he could not help expressing it forcibly.

"One cannot to-day (1896) imagine the state of surprise and even stupefaction into which doctors and students were thrown when, with a simplicity and assurance which seemed astonishing in one who was entering a maternity hospital for the first time, Pasteur criticized the methods of dressing, and declared that all the materials ought to be sterilized in an oven. Furthermore, he claimed that he could, by examining the lochia, point out those women who would have a rise of temperature, and stated that in a woman heavily infected he could demonstrate the microbe in blood from the finger. Pasteur did what he had said he could do. In spite of the tyranny of medical training which controlled original thought at that time, some students were carried away, and visited the laboratory to have a closer view of methods which made such accurate diagnosis and such sure prognostication possible.

Thanks to the methods inspired by Pasteur's work, maternity hospitals are no longer "ante-chambers of death," and epidemics of puerperal fever are found there no more.

CHAPTER XXVIII

CHICKEN-CHOLERA—ATTENUATION OF VIRULENCE—VIRUS VACCINES

" THERE sometimes appears in poultry-yards a destructive disease known by the name of chicken-cholera. The bird affected by it is feeble, and staggers about with drooping wings. Its ruffled feathers give it the shape of a ball. It is seized with overpowering somnolence, and if one forces it to open its eyes it appears to wake from a deep sleep; the lids soon close again, and usually death occurs after a short mute agony, without the creature having changed its position."

It was at the Academy of Science, February 9, 1880, that Pasteur drew this remarkable picture. It was thought, without positive proof, that this disease was caused by a microbe. Moritz, a veterinary surgeon of Haute-Alsace, was the first to see the microbe, in 1869. Peroncito, a veterinary-surgeon of Turin, had drawn pictures of it in 1878. In the following year, Toussaint, Professor at the Veterinary School of Toulouse, had insisted more emphatically on the parasitic nature of chicken-cholera, but he had not succeeded in obtaining subcultures of the parasite.

Pasteur had no trouble in finding the microbe: it appears in the form " of tiny bodies, extremely slender and constricted in the middle, which would at first sight be taken for isolated dots." Neutral urine, which was used by Toussaint, is a bad medium for cultivation; but broth made of chicken meat, neutralized with potash and sterilized at 120° C. is wonderfully favourable. The organism multiplies with a facility which is marvellous.

Pasteur also tried the yeast-fluid which he had used for his studies on fermentation, because he had found that all sorts of microbes, especially the anthrax bacteridium, are well suited by the pabulum which this fluid offers them. However, " this medium is absolutely unsuited to the growth of the microbe of chicken-cholera ; it actually dies there, promptly, in less than forty-eight hours. Is not this the exact counterpart of what one observes when an organism shows itself harmless to the animal into which it is inoculated ? It is harmless because it does not develop in the body of the animal, or because its development does not affect organs essential to life."

A few drops of the culture of the microbe poured on to the food given to chickens " suffice to convey the disease through the intestinal canal, where the microbe flourishes in such large numbers that the excreta of chickens so infected cause the death of others inoculated with them." It is mainly through the excreta of affected fowls that the disease is spread in the runs.

The inoculation of the microbe of chicken-cholera on adult guinea-pigs generally only causes an abscess, which opens of itself and is cured without visibly affecting the animal's health. " It is the growth of the inoculated microbe which causes the abscess, which acts as a closed vessel for the little organism, from which it is easy to obtain it without even killing the animal. It continues to exist mixed with the pus in a very pure state and without losing its vitality. The proof of this is that if one inoculates fowls with a little of the contents of the abscess they quickly die, whereas the guinea-pig which has provided the virus recovers without the least suffering.

" In this case one is dealing with a localized development of a microscopic organism which sets up a formation of pus and a closed abscess without causing internal disease or the death of the animal in which it is found ; nevertheless it is always ready on inoculation to carry death to animals of another species ; ready always even to cause the death of the animal in which it exists in an abscess if certain more or less accidental conditions bring about its passage into the blood or the splanchnic organs.

" Fowls or rabbits put with guinea-pigs suffering from abscesses of this nature might suddenly become ill and die, without the least alteration appearing in the health of the guinea-pigs. To bring about this result it would only be necessary that the abscess having opened should scatter a little of its contents on the food of the rabbits and fowls. Anyone observing this phenomenon and ignorant of the connection which I am describing would be astonished to see the rabbits and fowls decimated without apparent cause, and would imagine that the disease had arisen spontaneously, for he would never suppose that it owed its origin to the healthy guinea-pigs, especially if he knew that they also are subject to the same infection.

" How many obscurities in the history of contagions will one day be cleared up in ways even more simple than that which I have described ! Let us throw away theories which we can disprove with convincing facts, but not on the vain pretext that some of their applications are incomprehensible. The contrivances of nature are at the same time simpler and more diverse than those imagined by us."

These experiments throw a bright light on many obscure points in human pathology. Pasteur followed them, as he has been careful to say, with his pupils Chamberland and Roux.

They were interrupted by the vacation of 1879. On his return, Pasteur wished to continue his series of cultures ; he was disagreeably surprised to find that most of those which he had left behind were no longer capable of reproduction. Up till then successive transplantations at short intervals had produced broth cultures whose virulence continued without perceptible variation ; now the virulence was entirely gone : attempts at renewing it failed ; transplantations of old cellules into fresh broth no longer grew, and affected inoculated fowls very slightly if at all. It seemed that the incomplete experiments would have to be abandoned. This was very unfortunate and would mean a great waste of time.

Before making up his mind to it, Pasteur wished to try whether the inoculation of these sterile cultures had produced no change in the condition of the chickens which had resisted them so easily. He injected these chickens with a fresh culture, and performed the same operation on others fresh from the market and intended to act as controls. The latter died after the normal interval, whilst almost all the others proved resistant.

This was astounding. Pasteur had made the most wonderful of his discoveries. He had found out vaccination! And it was not mere chance, but a just reward: he was reaping the fruits of prolonged meditation on virulent diseases and on the work of Jenner.

At the very beginning Jenner had shown that cow-pox when inoculated on man protects him from small-pox. He believed that this disease had been transmitted to the cow by a cowman suffering from small-pox; but in that case inoculation of cow-pox ought to abolish small-pox, and the cow-pox also threatened to disappear, and even to go first, which would have been for a certain length of time a great misfortune. It was because of this fear that Jenner sought and found means of perpetuating the vaccine by inoculation from man to man; vaccine so obtained had a separate existence which could be indefinitely prolonged by a series of inoculations. This was the great discovery which made Jenner's name immortal.

Before this discovery, so-called *variolization* (inoculation of small-pox) was often practised. When, as is by no means uncommon, a mild case of small-pox was observed, the opportunity was taken to inoculate what it was thought ought to provoke a disease equally mild; but this hope was not always realized, and the cases when induced small-pox ended in death were innumerable.

The immunity which Pasteur had just obtained was analogous to that produced by inoculation of small-pox, but with this important difference, that the virus of variola and vaccinia are unknown, whereas the virus of chicken-cholera is a living thing which can be observed outside the body, which is easy to study in cultures, and which can be submitted to treatment.

One of the essential characteristics of virulent diseases is the absence of recurrence. It is exceptional to have small-pox, scarlet-fever or typhoid twice. Chicken-cholera, which cannot develop twice in the same animal, is therefore a virulent disease, against which protection can be obtained by artificial immunization. Pasteur must have trembled with joy when he saw his dream realized.

The attenuation of virulence had been obtained by the increased age of the culture. Pasteur wished to verify this fact.

When the time which elapses before an original culture is used to implant a second is varied from one day to two months, the virulence of the subculture remains apparently the same as the primary one. But in proportion as the interval is further prolonged the virulence is attenuated, and the inoculated fluid gives rise to a disease, developed with less rapidity and of a milder character. After intervals of three, five or eight months or more, the effect becomes more and more marked, mortality diminishes, and ends by being abolished. This decrease, however, does not follow a regular curve, and it must not be expected that it will be the same after equal intervals with successive cultures.

Diminution of virulence is due to the action of oxygen; and actually the same culture which is progressively attenuated in contact with air preserves its original virulence in a closed tube from which oxygen is excluded.

The virulence of a germ-culture can be measured by the results of its inoculation into animals; but allowance must be made for the fact that such a measurement is necessarily only approximate, because of all the individual variation in a group of animals taken haphazard and of vital phenomena in general.

In this way, by allowing oxygen to act for different lengths of time, one can obtain all degrees of virulence between that of a culture the inoculation of which is invariably fatal, and that which no longer produces any effect. By protecting cultures brought to different degrees of attenuation from the air it is possible to keep them in a fixed state at these degrees. And experiment shows that if a new fluid is sown with any particular culture, the degree of virulence of the parent culture persists in the subcultures so long as they are not made after too long an interval.

Émile Roux has expressed this admirably. "Attenuation," he says, "is hereditary. These viruses are microscopic vegetations; they can be modified by culture like the higher plants. Pasteur has obtained varieties of virus as a gardener raises varieties of flowers."

The new method had only an outward resemblance to Jenner's discovery; Pasteur distinguished the difference between the two thus: "The properly called virus-vaccine, that of Jenner, induces a benign disease, vaccinia, which protects from a more serious one, variola. In the same way the virus of chicken-cholera acquires states of attenuated virulence which give the same disease but not in a fatal form, with the result that after recovery the animal is able to withstand the inoculation of a very virulent virus.

Pasteur has even the right to add that the problem is better worked out in the case of chicken-cholera, because he knows and cultivates the virus; he knows that the attenuated virus is derived from the mortal virus, and he has grasped the degree of this attenuation, while the relation between variola and vaccinia are unknown, and no method has been discovered of changing one into the other.

It was in order to pay homage to Jenner that Pasteur gave the name of vaccination to a method of immunization which we really owe entirely to him.

The attenuated microbe of chicken-cholera keeps its modified virulence during passage from culture to culture. It is thus a true virus-vaccine, and this raised hopes of obtaining artificial cultures of all viruses and virus-vaccines of all acute infections.

Pasteur allowed no detail of his observations to be lost. He had noticed that in certain cases cholera, instead of killing quickly as is usual, passes into a chronic state, the fowls only succumbing after weeks and months of languor. During this time the parasite can be recovered from them, and, contrary to what might be expected, its virulence is greatly increased. The parasite has no doubt chanced on a vaccinated subject unsuitable for this reason to its active growth. "Such facts help us to understand the possibility of prolonged incubations of a virus, such, for example, as rabies, which, after having existed in the body for a long time latent, suddenly manifests its presence by most marked virulence and death."

It was not without intent that Pasteur mentioned rabies; he had already determined to tackle this terrible disease in the secret hope of conquering it.

CHAPTER XXIX

THE PROPHYLAXIS OF ANTHRAX

WHILE carrying on his splendid investigations on the vibrion-septique and on chicken-cholera, Pasteur continued the study of anthrax.

By finding the virus-vaccine of chicken-cholera he had made a magnificent discovery, but the disease in itself was not of great interest. The poultry-farmers had long known that to avoid the consequences of *epidemics* too many fowls must not be kept on the same site; they must be divided into larger or smaller groups in small runs; sick ones must be immediately killed or isolated. This is a sure means of limiting the spread of disease and avoiding heavy losses.

The same procedure can be employed to ward off anthrax. This disease attacks cattle and horses, but it is above all among sheep that it is most destructive. Some flocks are decimated; in some the mortality is as high as a third, or even half the animals. In the Beauce alone the annual losses amount to millions. The Minister of Agriculture asked Pasteur to study anthrax in sheep and cows as he had studied silk-worm disease.

Pasteur allied himself with Chamberland and Roux, two collaborators whose value and whose enthusiasm for work he appreciated, and who having been established near Chartres during the summer, could embark immediately on the necessary studies. Roux has given a lively description of this period of research.

" Every week Pasteur came to direct and follow the work. Those campaigns against anthrax in the country round Chartres have left us many pleasant memories. From early in the morning we visited the sheep-folds scattered over the great plateau of the Beauce, resplendent under the August sun, and carried out autopsies at the knacker's in Sours, at M. Rabourdin's, or in farmyards. In the afternoon we made notes of the experiments, wrote letters to Pasteur, and prepared for new investigations. The day was fully occupied, and how interesting and health-giving was this bacteriology in the open air!

"On the days when Pasteur came to Chartres, *déjeuner* at the Hôtel de France did not take long; we were soon off in a carriage to Saint-Germain, where M. Manoury had gladly put his farm and his flock at our disposal. During the drive we talked over the experiments of the past week and those which were to be undertaken. Pasteur, in a great hurry, hastened to the sheep-folds; motionless beside the hurdles, he observed the groups under experiment with a sustained attention which nothing escaped; for hours he followed with his eyes a sheep which he thought ill; he had to be reminded of the time, and shown the spires of Chartres disappearing into the night, before he could be induced to leave. He asked the farmer and his men questions; he always valued the shepherds' opinions, because, owing to their lonely life, they give all their attention to their flock, and often become wise observers."

Pasteur's first care was to seek the cause of what is called *spontaneous anthrax*, that which appears suddenly in a flock without contact with sick animals.

Koch had explained the persistence of the disease in an anthrax country by the resistance of the spores; he has shown that the malady develops as though it resulted from an infection by the digestive tract, and he had produced infection thus by giving guinea-pigs food sprinkled with bacteridium cultures. He had not experimented on larger animals.

Pasteur resolved to complete these experiments and to transport them from the laboratory to the natural habitat of the animals. He had said: "One method almost alone has served me as a guide to the study of micro-organisms. It consists essentially in the culture of these minute beings in a pure state, that is, freed from all other materials living or dead which accompany them.

By employing this method the most complicated problems sometimes receive simple and decisive solutions." It was once more from this method that he demanded the answer to his question about spontaneous anthrax.

To begin with, he fed certain lots of sheep on lucerne watered with cultures of anthrax bacteridia. In the same lot some sheep died with all the symptoms of spontaneous anthrax; most survived, often after having shown signs of illness. The mortality was increased by mixing with the lucerne dried thistle leaves and pieces of barley beard, all sharp substances that might erode the mucous membrane and so facilitate the entry of germs.

Eight sheep which had been used for these experiments were then inoculated with cultures, or even with anthrax-blood. All were ill, but only one died. Pasteur, recalling that fowls fed with food contaminated with the microbes of chicken-cholera could, when they did not die, be inoculated in this way, asked himself whether, by an analogous method, sheep could not be vaccinated. The experiment just made already provided an answer.

In the last hours of its life the blood of an animal only contains the bacteridium in the form of threads without spores; when the body begins to putrefy this bacteridium, deprived of oxygen, is not long in perishing.

Usually, however, at the moment of death the animal loses blood through the nose or mouth. When it is skinned the blood is spread freely on the soil, and this blood, mixed with air-containing earth, finds conditions favourable to spore production. Generally the carcass is buried, not very deeply, on the spot. Pasteur concluded from this that there ought to be spores on the surface of the graves, and he set himself to the task of verifying thishypothesis.

He suspended in water a little of the earth from a pit dug fourteen months before. It is with the finest particles which are last deposited that the microbes of cultivated soil will be found in milliards. If some of these were planted just as they are, the struggle for existence would certainly not allow any anthrax spores which might be found there to develop; but these spores easily resist a temperature of 90° C., which kills most soil microbes. It is sufficient to heat the fine particles of earth to this degree and then inoculate them into guinea-pigs to cause some to die of anthrax, and thus prove the existence of the spores.

These were interesting facts, but they did not completely satisfy Pasteur. How do spores remain on the surface of the soil, where they are swept by the rain and carried by the wind, if not buried by ploughing or other methods of cultivation? Pasteur continued to inquire. His collaborator, Roux, tells how he found the answer during one of his visits to the Chartres neighbourhood:

"The harvest was carried, nothing remained but stubble. Pasteur's attention was drawn to part of a field by a difference in the colour of the ground. M. Manoury explained that the year before some sheep which had died of anthrax had been buried on this spot. Pasteur, who always examined things closely, noticed on the surface of the ground a number of worm-casts. The idea occurred to him that the worms in their constant passage from below carried to the surface earth rich in the humus which surrounds a dead body, and with it the anthrax spores which it contains. . . . Pasteur never stopped short at supposition. He proceeded immediately to experiment. This confirmed his anticipation. It reminds me among other things of a demonstration given before Villemin, Davaine and Bouley. The last mentioned had taken the trouble to send for some worms collected from the earth of a pit where anthrax carcasses had been buried many years before. The earth from the intestine of one of the worms gave anthrax to guinea-pigs on inoculation."

These exhumed spores are eaten by sheep cropping the short grass; they can also be carried as far as the stream where the flock is watered, and may thus come in contact with a scratch which facilitates inoculation.

Pasteur had found the bacteridium in the earth of graves, and had also discovered that earth taken some yards away did not contain it; but he was never content with laboratory experiments. He had the place in a field where two years previously an anthrax cow had been buried enclosed. Four sheep were shut up there. Four other sheep, intended as controls, were placed in a similar enclosure some yards from the first and rather higher up. Eight days later one of the sheep in the first enclosure died of anthrax. The control sheep remained perfectly well.

A note written fifteen years before by Baron von Seebach, Saxon Minister in Paris, had given evidence of the same nature. According to this note, which was addressed to the Minister of Agriculture and which Pasteur's experiment recalled to memory, one of the Baron's tenants wished to have spread in his stables some earth coming from a field where from time immemorial anthrax animals had been buried. Owing to the protests of the shepherd, the earth was only taken into one half of the stable; in this part there happened to be nine hundred sheep. In a fortnight three hundred and twelve had died of anthrax. Eight died in the adjoining enclosure, and not one in the third, which was not in contact with the first.

In addition to this the Baron had noticed a little corner in one of his fields where the clover had grown with extraordinary vigour, making a beautiful contrast with the sparse vegetation surrounding it. He learnt that some anthrax sheep had been buried there. This clover was stolen by a woman, who fed her goat and cow with it. The cow was very ill, and the goat died.

These different observations already formed a certain basis for prophylaxis against anthrax. It was proved necessary to destroy the bodies of animals which had died of it, or at least to fence off their graves, for it is they which form the sole danger of *accursed fields*

CHAPTER XXX

ATTENUATION AND REINFORCEMENT OF VIRUS

The Minister of Agriculture had asked Pasteur to give an opinion on a method of treating anthrax devised by a veterinary surgeon of the Jura. The treatment was found useless, but the experiments made in connection with it had a useful result in providing Pasteur with two cows cured after a severe attack of anthrax. A month later Pasteur inoculated them with a very virulent culture; they were quite unaffected. Anthrax, therefore, does not recur. It resembles in this chicken-cholera, and it ought to be possible to discover a vaccine.

The microbe of chicken-cholera increases solely by division, and does not appear to form spores.

In a new culture the bacteridium begins by multiplying in the same way; but after from twenty-four to forty-eight hours one sees individuals—and especially those in contact with air—change into oval, very refringent globules, which are gradually set free and form true spores. Observation shows that these spores can be exposed to air for any length of time without undergoing any alteration either of vitality or virulence.

In its filamentous form, and during multiplication by fission, the bacteridium may be compared to a plant reproducing itself by budding. A seed remains unaffected by the action of air, but a bud left on the ground in contact with air soon dies. For this reason, if one is to employ the action of oxygen on the bacteridium with effect, means must be found to prevent spore formation.

This can be achieved by various means. In neutral chicken-broth the bacteridium never grows below + 16° C., nor above 44°; at these extreme temperatures spores never form. Between 43° and 42° growth is rapid and abundant, but still no spores are found. If this temperature is maintained for about a month, the vitality being tested by daily subculture, one finds one day that the culture kept in contact with air is dead: that is to say, that if planted in fresh broth it no longer grows. However, on each of the days preceding that on which sterility appears the culture was steadily reproduced: death has occurred suddenly. The virulence has not behaved in the same way as the vitality; it slowly dininishes. After a week of exposure to 42 to 43° C. it is destroyed, or at least the culture has become harmless to the sheep, the rabbit and the guinea-pig, three animals very susceptible to anthrax.

By studying the series decreasing in virulence, Pasteur obtained a bacteridium without action on any known animal, whatever its age. It is very certain that if one met such a microbe occurring naturally, without knowing its source, no one would recognize it as a degenerate descendant of a virus which was virulent and which could become so again.

Again, immediately before this bacteridium, deprived of all virulence, one finds another which kills a guinea-pig one day old but is harmless to older animals. "If one transfers it from the day-old guinea-pig to another, by inoculating the blood of the first into a second, from this to a third, and so on in succession, one progressively reinforces the virulence of the bacteridium—in other words, its ability to develop in the organism. Soon, as a result, it can kill guinea-pigs three or four days, a week, a month or many years old, or even a sheep. The bacteridium has regained its original virulence."

In the same way the microbe of chicken-cholera can be attenuated so as to render it harmless to the adult animal. At this time it still kills small birds, such as sparrows and canaries. By successive passages through the bodies of these birds, one can gradually bring back the virulence which will again enable it to kill fowls.

These facts seem to account for the so-called *spontaneous* nature of certain epidemics: an epidemic which has died out owing to the attenuation of its virus can be reborn under certain conditions by the reinforcement of that virus.

After having settled the means of prophylaxis against anthrax, Pasteur pointed out ways of making animals refractory to virulent inoculations. He said: "Before the virulence is destroyed, the anthrax microbe passes through different stages of attenuation; and besides, as in the case of chicken-cholera, each of these states of virulence can be reproduced by cultures. In short, as anthrax is not a recurrent disease, each of our attenuated anthrax microbes acts as a vaccine for a microbe of greater virulence, that is to say, one capable of causing a more benign disease. What could be easier than to find among this series of viruses ones suitable to produce anthrax fever in sheep, cows and horses without destroying them, and able to preserve them in future from a fatal disease? We have practised this operation on sheep with great success, and as soon as the time comes for penning these animals on the Beauce we shall test its application on a big scale."

CHAPTER XXXI

VACCINATION AGAINST ANTHRAX

Pasteur's communication to the Academy of Science made a great sensation. Many of the veterinary surgeons could not peacefully submit to this invasion of their domain by an outsider. Farmers, so often deceived by offers of new and infallible remedies, wondered how much truth there was in this hope held out to them of the conquest of anthrax, and quite an agitation arose to put the *inventor* on his trial, that he might either prove his statement or have the falsity of his promises publicly demonstrated.

However, six months after Pasteur had made known his virus-vaccine against chicken-cholera, Toussaint, a professor at the Veterinary College of Toulouse, announced that he had discovered a sure means of vaccinating against anthrax. He used anthrax-blood, which after defibrination he treated in two ways: by filtration through many thicknesses of paper, or by heating at 55° C. for ten minutes.

Toussaint believed that the bacillus anthracis forms, in the blood of the animals in which it develops, a material which can become a vaccine against itself. The problem was to isolate this material. Toussaint said that he succeeded in doing this by filtration, which removes the bacteridium, or by heating, which kills it.

Pasteur was much upset by the publication of these results, which directly contradicted his doctrine: the new virus was no longer a living being which can be cultivated, but a soluble, inert substance which passes through a filter. This happened in the middle of the vacation of the year 1880. Pasteur at once called for his faithful Chamberland and Roux, who did not hesitate to return to work with him. They soon saw that Toussaint had interpreted his results wrongly.

Filtration is always ineffective: either the defibrinated blood gives anthrax and kills, or it does not do so, and produces no immunity.

The bacteridium heated to 55° C. is not killed with certainty. If it is killed it is easy to verify the fact by a test culture, the liquid by itself having no immunizing action. If it is not killed, it may be modified as regards vitality, and then possesses either an altered virulence which kills, or an attenuated one which protects; but this can only be ascertained by experiment. In the case when attenuation does exist it cannot be fixed by culture; it may disappear after having been demonstrated, and the method is always dangerous. A test experiment tried at Alfort showed this clearly. Anthrax blood defibrated and heated at 55° was inoculated into twenty sheep; four rapidly succumbed, and the others were so ill that it was feared that they would all die.

On March 21, 1881, Pasteur made known to the Academy, in his own name and in those of his collaborators, Chamberland and Roux, the methods employed to prepare virus-vaccine.

He chose a very virulent bacteridium. On January 28th the broth in which this was planted was placed in an incubator kept at 42 to 43°. By February 9th, after twelve days' exposure to this temperature, it was already incapable of killing adult guinea-pigs. On the 28th a culture sown from the broth, kept at a temperature of 42 to 43°, still killed young mice but not guinea-pigs. On March 12th a fresh culture was harmless even to mice and guinea-pigs twelve hours old.

A virus can thus be prepared of all degrees of attenuation. These viruses undergo alteration into spores, and these spores on cultivation reproduce the virulence of the attenuated bacteridia from which they are derived. One has therefore "virus-vaccines fixed as spores with their particular characteristics, which can be transported without possibility of change," and which permit the immunization of all animals susceptible to anthrax according to methods determined for each species. Sheep present great variations in their individual susceptibility, "therefore in practice one makes two inoculations at twelve days interval, the first with a very feeble virus, the second with a stronger one, which completely immunizes" (Roux).

Pasteur was not obliged to await the penning time of the sheep to make the trials he had spoken of at the Academy of Science. Roux, his collaborator, has given a most interesting account of the experiment performed at Pouilly-le-Fort, near Melun.

"The Agricultural Society of Melun suggested that Pasteur should give a public demonstration of the new method. The programme was made out on April 28, 1881. Chamberland and I were on a holiday; Pasteur wrote to us to return immediately, and when we were again assembled in the laboratory, read out to us what had been arranged. Twenty-five sheep were to be vaccinated, and afterwards inoculated with anthrax at the same time as twenty-five controls; the first lot were to resist, the second to die of anthrax. Every detail was definitely settled. There was no margin for the unexpected. On our remarking that the programme was a stiff one, but that there was nothing to be done but to carry it out as the agreement was already signed, Pasteur answered: 'What succeeded with fourteen sheep in the laboratory will be equally successful with fifty at Melun.'

"The animals were collected at Pouilly-le-Fort, near Melun, on the property of M. Rossignol, a veterinary surgeon, who had proposed the experiment and who was to superintend it. 'Whatever you do, don't mix up the capsules!' said Pasteur gaily, when, on May 5th, we left the laboratory to go and make the first vaccine inoculation.

"That of the second vaccine was made on the 17th, and every day Chamberland and I went to visit the animals. During these repeated journeys from Melun to Pouilly-le-Fort plenty of remarks reached our ears which showed that not everybody believed that we should succeed. Farmers, veterinary surgeons and doctors followed the experiment with lively interest, some even with passion. In 1881 the science of microbes had no supporters; many thought the new doctrines pernicious, and thought it a lucky chance which gave them an opportunity of attacking Pasteur and his assistants outside the laboratory, and confounding them in the daylight of a public experiment. They thought that they were about to destroy with one blow these innovations which were compromising medicine, and would regain the security of healthy traditions and old customs just at the moment when they were threatened!

"In spite of the high feeling which was raging round the experiment, it continued its course. The test inoculation was made on May 31st, and a meeting arranged for June 2nd to record the results. Twenty-four hours before the decisive moment, Pasteur, who had undertaken the public experiment with such perfect confidence, began to regret his boldness. For some moments his faith faltered, as if it might be possible for the experimental method to betray him. Too long a mental tension had brought about this reaction, which, however, did not last. The next day, with more assurance than ever, Pasteur was going to record the brilliant success which he had predicted. In the crowd which thronged that day at Pouilly-le-Fort there were no more unbelievers, but only admirers."

As a fact, of the non-vaccinated sheep twenty-two were dead, two dying, and the last so ill that it died before night. The vaccinated all appeared to be in good health.

At the request of the Agricultural Society of Melun the experiment had been extended to ten cows, of which four were vaccinated, while the others served as controls. All received the very virulent vaccine at the same time as the sheep. In spite of the fact that these studies were not as far advanced for cows as for sheep, Pasteur had declared that the six vaccinated cows would not be affected, whereas of the four others some or all would die, and in every case would be very ill.

"This prediction," said Pasteur, "had a boldness which only a brilliant success could justify. Many people were so kind as to suggest this to me, adding some reproaches concerning the rashness of science."

The rashness was indubitable. Pasteur had himself noted, when attempting to measure the degree of virulence of a culture by the result of its inoculation on animals, that the measurement is necessarily only approximate, owing to individual variation in a group of animals taken haphazard, and in vital manifestations in general; but he had faith, he wished to convince, and he knew that conviction cannot be carried to a crowd by promises qualified by too many reservations.

His prophecies were realized with the cows as with the sheep. Such was the enthusiasm that one of the veterinary surgeons who had in the beginning been most sceptical wanted to have himself vaccinated and then tested with the most virulent virus.

One of the vaccinated sheep died on the 3rd of June. The autopsy, made the same day by two veterinary surgeons, showed the sheep to be pregnant and at full time. The lamb had been dead twelve or fifteen days. Their opinion was that the mother's death was caused by that of the lamb. The death of the latter must have occurred between the 19th and 22nd of May. Now the second vaccination took place on the 17th. In order to follow its effects the temperatures of the animals were taken daily. Taking a sheep's temperature is not an easy matter; it has to be turned over on the ground, and kept still in spite of its struggles for some minutes. The farm lads who were entrusted with this duty were sometimes rather brutal; it was very likely that the lamb's death was due to an incident of this kind. The blood of this sheep which had died after inoculation was examined microscopically, and cultures were made which failed to reveal bacteridia.[1]

Pasteur ended his communication to the Academy of Science by saying: "We now possess virus-vaccines against anthrax capable of preventing a fatal attack, and never being themselves fatal; living vaccines which can be cultivated at will, carried everywhere without alteration, prepared, in short, by a method which we believe capable of generalization, for it was first used to discover a vaccine against chicken-cholera. From the nature of the conditions which I here recount, and looking at things only from the scientific point of view, the discovery of anthrax vaccine represents a distinct advance when compared with Jenner's vaccine, because the latter has never been obtained experimentally."

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[1] Dr. Emile Roux, oral communication.

However, all Pasteur's opponents were not convinced. "That which was inoculated at Pouilly-le-Fort," they said, "was not anthrax-blood, the deadly poison which defies all remedies, but a mixture of unknown nature made up in a laboratory, and whose constitution no one knows but the makers." Another experiment was made near Chartres. Thirty-five sheep, nineteen vaccinated and sixteen controls, each received ten drops of blood from a sheep which had just died from anthrax; the fifteen controls died, all the vaccinated stood the test perfectly. Those who could not see after this were only the wilfully blind.

In the very next year the Veterinary Society of Chartres published the results of a first anthrax vaccination campaign. Some of the figures especially attracted attention. Part only of certain flocks had been vaccinated. Vaccinated and non-vaccinated continued living together under the same conditions. The comparison between the two groups was particularly instructive. In these flocks, of 2,308 vaccinated there were 8 deaths; of 1,659 non-vaccinated there were 60 deaths, that is 0·6 per cent., or—to avoid dealing with fractions—the numbers can be recorded as though, for two equal lots of 10,000 sheep, there were 34 deaths in the vaccinated and 360 among the others.

The fame of the Pouilly-le-Fort experiments spread far and wide and provoked real enthusiasm throughout France. The *Grand Cordon* of the Legion was offered to Pasteur, and he asked for and obtained the Riband of Chevalier for his collaborators, Chamberland and Roux.

This year of 1881 was for Pasteur one of overwhelming work. To an always busy life in the laboratory, where work had just been started on the study of rabies, and where he was already occupied with *rouget*, he had to add the preparation of anthrax vaccine, the superintendence of experiments started all over the country, and correspondence with those who were conducting them, which included requests for information, thanks, and sometimes complaints following on badly-carried-out operations. Pasteur was equal to it all, and displayed once again during this victorious campaign those gifts of leadership which he had already shown when he had to defend, in the interest of agriculture and of science, his method of preventing silk-worm diseases.

The victory was won, but certain adversaries remained unsubdued. To one of these, who pursued him with attacks before the Academy of Medicine, Pasteur replied with justifiable pride: "I should have been inconsolable if this great discovery of vaccine had not been made by a Frenchman."

Pasteur had shown that the blood of an animal which had died of anthrax twenty-four hours previously contained both the bacteridium and the vibrion-septique. It was because they had not taken this fact into consideration that the professors of the Veterinary School of Turin obtained very bad results from a vaccination experiment made in 1882. All their animals, vaccinated and unvaccinated, which were inoculated with the blood of an animal which had died of anthrax, perished. The inoculation had been made more than twenty-four hours after the animal's death. Pasteur declared that in so doing they had made a very serious mistake, and gave his reasons. The professors of Turin replied rudely by a letter communicated to most of the European scientific journals and to a number of scientists. They certified that they had found no evidence of septicæmia either in the sheep used for the test inoculations or in the animals which died as a result of this inoculation. Moreover, they considered it miraculous that "His Lordship" could affirm the existence of this disease in an animal which he had not seen. Pasteur offered to go to Turin and prove there that in any animal whatever killed by anthrax, the blood, containing originally only anthrax, would on the following day contain both anthrax and septic organisms.

Roux was employed to prepare the experiments which were to be repeated before the professors of Turin. Pasteur has given a detailed account of one of them :

"On May 5th of this year (1883), at seven o'clock in the morning, a sheep died from anthrax. The mean temperature was 11° C. ; the evening and night were warmer and also stormy. On May 6th, just twenty-four hours after death, an autopsy was made, and blood taken from the heart. A drop of this blood was sown in sterile broth, in one case aerobically, in the other in tubes suitable for anaerobic culture. The same blood was, in addition, inoculated into a sheep. Next day the aerobic culture showed anthrax bacteridia, and when inoculated into guinea-pigs killed them with simple anthrax. The culture *in vacuo* was, on the contrary, *septique*, and when inoculated into guinea-pigs gave them a most acute septicæmia, which killed them in twenty-four hours.

"The sheep inoculated with heart blood died in the same way from septicæmia the day after inoculation.

"In short, when a sheep dies from anthrax, and when it has already become infected both with anthrax and septic organisms, one can easily obtain from its blood anthrax and its microbe, and also septicæmia and its microbe.

"The presence of air in contact with a fluid culture of small depth prevents the development of the vibrion-septique, because these are aerobes ; the presence of air is favourable to the bacteridium. The bacteridium cannot do without air for its development and multiplication. Air would destroy the vibrions, on the other hand, if they did develop, but culture *in vacuo*, or in the presence of nitrogen or pure carbonic acid, allows their development."

Had Pasteur's offer to allow the professors of Turin to be witnesses of this experiment been accepted, there would have been an end of the dispute. The offer was, however, rejected, and this caused a long controversy which attracted more attention than it deserved.

The discovery of virus-vaccines, and the work which had led up to it, had made Pasteur world-famous to an extent of which he had no suspicion.

In August, 1881, he was entrusted with the official representation of France at an International Medical Congress which was to be held in London. The Prince of Wales presided at the opening ceremony. When Pasteur entered the big St. James' Hall, and was conducted by one of the committee to the platform, there was great applause, mingled with *vivas* and hurrahs. Pasteur said rather nervously to his son-in-law: "No doubt that is the Prince of Wales arriving. I ought to have come earlier." The President of the Congress, Sir James Paget, replied: "But it is you whom they are all cheering."[1]

In 1884 the famous University of Edinburgh celebrated its third centenary. Each section of the *Institut Français* had nominated one or two members to represent it at this celebration. Pasteur and Ferdinand de Lesseps were the delegates of the Academy of Science.

Pasteur, on his arrival in London, had the pleasant surprise of finding himself invited, with his colleagues, to occupy a saloon-carriage put at their disposal by Mr. Younger, an Edinburgh brewer, who wished to express in this way his thanks to the scientist whose studies on beer had contributed so largely to the prosperity of his firm.

The University followed the old custom of bestowing a certain number of degrees of Doctor of Law and of Theology on the most distinguished guests, and Pasteur was made Doctor of Law.

After the imposing ceremony at which the diplomas were presented, a thousand guests assembled at a great banquet. When the time for toasts arrived, the Chancellor of the University read a telegram from the Queen conveying her congratulations to the noble institution on its third centenary, and her best wishes to all connected with it. The first toast drunk was that to the Queen and Royal Family.

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[1] René Vallery-Radot, *op. cit.* p. 466.

When Pasteur's turn came to speak, he rose and said:

"My Lord Chancellor and Gentlemen, the town of Edinburgh presents a spectacle of which it may well be proud. All the representatives of great scientific institutions here gathered together appear like a great congress of congratulation and hope. The honour and glory of this international gathering are yours by right. For centuries Scotland has linked her destiny with that of human intelligence. She was one of the first among the nations to understand that intellect leads the world; and the intellectual world, answering your appeal, pays you the homage you deserve. Yesterday, when under the vaulted roof of St. Giles, the eminent Professor Robert Flint, addressing the University of Edinburgh, exclaimed: 'Remember the past, and look to the future!' all the delegates, seated like judges at a great tribunal, evoked the past centuries, and wished with one accord that the future might be even more glorious than the past. In the midst of the delegates of all nations, who bear illustrious witness to their sympathy, are those sent by France from such institutions as best represent French genius and are her greatest glory. Wherever in the world a flood of light breaks forth France applauds; and when on foreign soil death strikes down a man of genius France mourns for him as for one of her children. This noble unity I have realized on hearing many of your men of science speak to me with emotion of the death of that famous chemist, J. B. Dumas, a glorious member of all your Academies, and not many years ago an eloquent eulogist of your own great Faraday. By leaving Paris I had the great grief of not being able tt follow his coffin to the grave; but the hope that I migho here render a last solemn homage to this revered master, this great citizen of France, has allayed my sorrow. Moreover, gentlemen, though men may pass away, their work remains. We are all but passing guests in those great domains of intellect which, like all the Universities which salute you on this solemn day, are assured of immortality."

These words were received with prolonged applause.

CHAPTER XXXII

PASTEUR AT THE ACADÉMIE FRANÇAISE

Pasteur wrote simply in order to explain his ideas and his discoveries, without any seeking after literary effect. Nevertheless several members of the Académie Française appreciated his *communications*, not only for their valuable substance but for their clear and exact form. They wished to nominate Pasteur in the place of Littré, who had just died.

Pasteur, at first rather astonished at the offer of an honour of which he had never dreamed, began paying the customary calls on the Academicians. He met with the kindest reception everywhere, though Victor Hugo asked him: "What would you say if I presented myself at the Academy of Science?" The great poet was sometimes a little slow of comprehension. Alexandre Dumas, on the other hand, refused to receive Pasteur's visit, saying: "It is I who will go to thank him for kindly consenting to be one of us."

Pasteur was elected on December 8, 1881.

The study which he was obliged to make of the life and works of Littré inspired him with the highest esteem for his predecessor; but nevertheless in his speech on his reception, he did not conceal the fact of the difference in their philosophical opinions.

Littré had been the "sincere and steadfast apostle of positivism." Pasteur confessed that he did not share Littré's appreciation of Auguste Comte:

"The cause of this difference seems to me to lie in the very nature of the work which occupied his life in contrast with that which is the sole object of mine.

"M. Littré's work was concerned with researches into history, language, and scientific and literary erudition. The stuff for such studies is found entirely in facts belonging to the past, to which nothing can be added or withdrawn. For this a kind of observation which as a rule can give no absolute demonstration suffices. The peculiar quality of the experimental method on the contrary is that it admits of no other.

"The experimenter, a man who achieves conquests over nature, finds himself constantly grappling with facts which are not yet manifest, and which for the most part only exist potentially in natural laws. The unknown in what is possible, and not that which has been, that is his domain, and in order to explore it, he has the help of this marvellous experimental method of which one may truthfully say, not that it is all-sufficient, but that it rarely deceives anyone, and then only those who use it wrongly. It eliminates certain facts, calls forth others, questions nature, forces her to answer, and only pauses when the mind is entirely satisfied. The charm of our studies, the enchantment of science, consists, if I may so express myself, in the fact that we are able, everywhere and always, to justify our principles and prove our discoveries.

"The mistake of M. Comte and M. Littré is to confuse this method with the limited method of observation. Both being strangers to experimentation, they give the word *expérience* the meaning it has in ordinary conversation, which is not the sense in which it is used in science. In the first case *expérience* is only simple observation of things and inductions drawn from them, more or less legitimately, as to what has been and what might have been. The real *experimental* method never stops short of undeniable proof.

"The conditions and results of the daily work of a scientist, moreover, accustom him to regard the idea of progress as that of discovery only. My first thought, then, in judging of the value of positivism was to find out how it was discovered. This I was unable to do. It is useless to talk of the discovery of the so-called law of the three states of the human mind[1] any more than of the hierarchical classification of sciences; neither the one nor the other can be more than approximations of little value. Positivism, offering me nothing in the way of a new idea, has left me cautious and distrustful.

"M. Littré's faith in positivism is due to the satisfaction he derives from it in great metaphysical questions. He was obsessed with negation as with doubt. Auguste Comte rescued him from both by a dogmatism which over-ruled metaphysics.

"In face of this doctrine, M. Littré said to himself: You do not need to concern yourself with the origin nor with the beginning of things, nor with God and the soul, nor with theology or metaphysics; follow your bent as a seeker 'restless or fascinated'; flee the absolute, love only the relative. What peace for this ardent soul which longed to explore every field of knowledge!

"A mistake has, however, been made about this tranquillity, and quite a false impression been obtained, in imagining M. Littré as a calm and convinced atheist. He was not callous with regard to the religious beliefs of others. 'I have,' he said, 'realized too deeply the sorrows and sufferings of human life, to wish to deprive anybody of convictions which help to sustain them under these trials.' He denied the existence of God no more than the immortality of the soul; he only reduces it *a priori* to an idea, because he says that it cannot be proved like a scientific fact.

"I, who consider the words progress and discovery synonymous, ask myself on the strength of what new discovery, philosophic or scientific, can one take from the human soul these uplifting beliefs. They seem to me essentially eternal, because the mystery which surrounds the universe is itself eternal in its nature. . . .

"Experimental science is essentially positivist in the sense that it never allows consideration of the essence of things, of the origin of the world and its destiny, to enter into its conceptions. It has no need of this. It knows that it has nothing to learn from metaphysical speculation. Nevertheless it does not avoid hypothesis. No one makes greater use of it than the experimentalist, but only as a guide and spur to research, and under the strictest control. He disdains and rejects his preconceived ideas the moment that experiment shows them not to correspond with objective realities. . . ."

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[1] The theological, the metaphysical, and the positive.

"M. Littré repeatedly defines positivism from the practical point of view thus: 'I call positivism all that is done in society to organize it according to the positive, that is to say the scientific, conception of the world.'

"I am willing to accept this definition, provided that it is strictly applied; but the great and visible gap in the system is this, that the positivist conception of the world does not take into consideration the most important of positive ideas, that of the infinite.

"Beyond that starry vault what is there? New starry skies? So be it! And beyond them? The human mind, urged by an irresistible force, will never cease asking: And what is there beyond that? Can there ever be an end to time or space? An end proves a limited greatness, simply greater than what has preceded it, and hardly has one begun to contemplate it, than the inevitable question returns, and the cry of curiosity can never be stifled. It is no use replying: beyond is space, time, or greatness illimitable. Nobody can understand such words. He who proclaims the existence of the infinite, and no one can escape this, accumulates in this statement more of the supernatural than is contained in all the miracles of all countries, for the idea of the infinite has the double character of being unavoidable and incomprehensible. When this idea takes possession of the mind, there is nothing left but to prostrate oneself. Again, at this moment of poignant suffering, pardon must be asked of reason: all the springs of intellectual life threaten to be relaxed; one feels oneself near the 'sublime folly' of Pascal.

Positivism gratuitously ignores this primitive and primordial idea with all its consequences on social life.

"Everywhere in the world I see the expression of the idea of the infinite. Owing to it, belief in the supernatural is found at the bottom of every heart. The idea of God is a form of the idea of the infinite. As long as the mystery of the infinite weighs upon human minds, so long will temples be raised to the cult of the infinite, whether the God be called Brahmah, Allah, Jehovah or Jesus; and on the pavement of these temples you will see men kneeling, prostrate, sunk in the contemplation of the infinite. Metaphysics only serve to translate within us the dominating idea of the infinite. Is not the conception of an ideal a faculty, a reflection from the infinite, which in the presence of beauty carries us on to imagine a still greater beauty? Science and the passion for knowledge, what are they but the spur which the mystery of the Universe applies to our souls? Where are the true sources of human dignity, of liberty and modern democracy, if not in the idea of the infinite before which all men are equal? . . ."

The Greeks felt the mysterious power of the infinite verities which we suspect without thoroughly understanding. "It is they who have bequeathed to us one of the most beautiful words in our language, the word enthusiasm—*’Εν Θεός*—an inner God.

"The greatness of human actions is measured by the motive which inspires them. Happy are those who carry within them a God, an ideal of beauty, which they obey: the ideal of art, the ideal of science, the ideal of country, the Gospel ideal of virtue. Those are the living sources of great thoughts and great actions. All are lit by reflections of the infinite.

"M. Littré had his inner God. The ideal which filled his soul was that of a passion for work and of love for humanity.

"I have often represented him to myself, seated beside his wife, as in some picture of the early Christians; he, looking at the ground, full of pity for the suffering; she, a fervent Catholic, with her eyes raised to heaven; he, inspired with all the natural virtues; she by all the supernatural; the two uniting in one impulse, as in one heart, the two flames which form the halo of the Man-God—love of man and love of God; she a saint in the canonical sense, he a lay saint.

"I have not originated this last expression. I heard it on the lips of all who knew them."

Pasteur did not hide his convictions. He had emphatically declared them in a speech made at the distribution of prizes at the College of Arbois, in giving his views on true freedom of thought:

". . . Do you know what most free-thinkers demand? It is for some the liberty of not thinking at all and of being enslaved by ignorance, for others the liberty of thinking wrongly; for yet others the liberty of being dominated by the suggestions of instinct and of despising all authority and all tradition. Free-thought in the Cartesian sense of the word, liberty in effort, liberty in research, the right to draw conclusions from truths proved by evidence and to regulate one's conduct by it, oh! let us have a cult of *that* liberty; that is what has formed modern society in all that it possesses of nobility and fertility; but free-thought which claims the right of forming conclusions with regard to what is not really understood, the liberty which implies materialism or atheism, that liberty let us emphatically repudiate.

"I really admire the great philosophers of these nihilistic systems which flourish nowadays! What? We poor patient observers of nature, rich in the discoveries of our predecessors, furnished with the most delicate implements, armed with the strictest experimental method, we stumble at every step in our search for truth, and we find that the material world, in the least of its manifestations, is nearly always different from what we expected. But they, given up entirely to fixed ideas, placed behind the impenetrable veil which covers the beginning and end of things, what do they do in order to obtain knowledge?

"Believe me, in the face of these great problems, these eternal subjects of man's solitary meditation, there are only two attitudes of mind: one created by faith, the belief in a solution given by divine revelation, and that of tormenting the soul by the pursuit of impossible explanations, expressing this torment by absolute silence, or by what comes to the same thing, by admitting the impossibility of understanding or knowing anything of these mysteries. Only a misguided mind tries to introduce religion into science. More misguided still is he who attempts to introduce science into religion because he entertains greater respect for the scientific method. The man who has religious faith does not know and does not want to know. He believes in a supernatural revelation. You will say that this is incompatible with human reason; I agree with you, but it is even more incompatible with human reason to believe in the power of reason to deal with the problems of the origin and end of things.

"And then reason is not everything: there is feeling, and what will always give strength to the convictions of a religious man is, that the teachings of his faith are in harmony with the natural impulses of his heart, while the belief of the materialist imposes theories repugnant to human nature. Does not good sense and the inmost feeling of each one proclaim individual responsibility? Materialism, on the contrary, rejects it. Beside the couch of a beloved one who has just been taken from you by death, do you not feel something within you which cries out that the soul is immortal? It is an insult to the heart of man to say with the materialists: 'Death is extinction.'"

Pasteur was a man of strong convictions strongly expressed. Renan was just the opposite. Entrusted on account of his position as Director of the Académie

Française with the task of replying to Pasteur, he addressed a delightful speech to him.

After a few words of greeting and of praise pronounced with accomplished elegance, he continues :—

" See, Sir, what strange people we are, and what irony seems attached to our efforts. Even in the matter of truth our qualities are even less useful to us than our defects. One must not be too perfect. If M. Littré had been less sincere he might have avoided some mistakes. The defects in his philosophy were those of a too timid soul. . . . He feared to appear to discount what he desired, and to be too ready to accept as a reality what was in truth only right. This hesitation implied a far more delicate cult of the eternal truths than the bold solutions which immediately satisfy superficial intelligences ! Truth is a great coquette, Sir ! She does not care to be pursued with too much passion. Indifference often succeeds better with her. When you think you hold her, she escapes you, if you wait she yields. It is when one thinks that one has bidden her farewell, that she reveals herself ; she keeps you at a distance, on the contrary, if you are too much in earnest, that is to say if you love her too much. . . .

" I will make a confession to you : in politics and in philosophy, when I find myself in the presence of incomplete ideas, I always agree with my interlocutor. inter
In these delicate matters everyone has some degree of right on his side. It is polite and just to seek in the opinion offered you only the amount of truth which it contains. . . .

" You prefer another philosophy to that of Littré, one which you suppose will find a ' last refuge ' here. Ah ! do not count too much upon that, Sir. The zone of our literary patronage is very wide. It extends from Bossuet to Voltaire. We often like to give sanctuary to the defeated ; the cause which should find a last refuge here might well be in very bad case. We do not protect doctrines, we discern talent. That is how we never have to make retractions or denials. Everything passes away but we do not pass away, for we are dependent upon only two things, which we trust will last for ever in France: intellect and genius. We respect every form which clothes a noble belief. You, for example, use two terms which I should never employ: idealism and materialism. The end of the world is the idea; but I know of no case in which an idea can be produced without material; I do not know any pure spirit, nor any work of pure spirit. The divine work is accomplished by the inborn tendency towards the good and the true which exists in the universe; I do not know whether I am a materialist or an idealist.

"It is prudent not to associate the end of moral beliefs with any system. The answer to the riddle which troubles and fascinates us will never be given us. As for myself, when anyone denies these fundamental dogmas, I feel inclined to believe them; when they are stated otherwise than in beautiful poetry, I am seized with unquenchable doubts. I am afraid of making too sure of them, and like the mystic described by Joinville, I am sometimes inclined to destroy heaven for love of God. It is doubt for which one deserves credit. . . ."

There are in the intellectual order, "apparent contradictions which do not exclude similarity. There are minds which are as impossible to bring together, as—to make use of a favourite comparison of your own—to put two gloves one into the other. And nevertheless both gloves are equally necessary; each is the complement of the other. Our two hands cannot be superimposed one upon the other, but they can be joined. In the great womb of nature the most diverse forces join and combine to bring forth a result of majestic unity. . . ."

Littré "was convinced that it is the tolerant who will inherit the earth, and that liberalism which is not afraid of the liberty of others has the mark of truth."

In 1872, while visiting a lighthouse on the coast of Brittany, he fell from the second story, but escaped with a few bruises; a local journalist regretted that he had not broken his neck. "We thought differently on theological questions," said M. Littré when telling the story, "and this was the way in which his disagreement expressed itself. . . ."

"Your absolute devotion to science gives you, Sir, the right to succeed such a man and to recall his great and hallowed memory to our minds. You will find in our meetings relaxation for a brain continually occupied with fresh discoveries. . . . You will observe with some interest the efforts of our critical philosophy to make allowance for error, by distrusting its proceedings and limiting the scope of its own statements. Seeing how much may be taught even by apparently frivolous literature, you will get to believe that the discreetly expressed doubt, the smile, the delicate wit of which Pascal speaks, may have their value. You will not have experiments to make here, but that simple observation of which you speak so ill, will suffice to procure you some very pleasant hours. We will communicate some of our diffidence to you, and you will give us of your assurance. You will, above all, bring us your glory, your genius, and the fame of your discoveries.

"Sir, you are welcome."

CHAPTER XXXIII

ROUGET

Rouget, or red-disease of pigs,[1] is a widespread and very serious disease. American statistics put the losses sustained through it in the United States during 1879 at 900,000. In 1882 in the valley of the Rhone alone 20,000 pigs died of it.

In March, 1882, Thuillier, one of Pasteur's collaborators, had gone at his chief's request to study this disease in a district in Vienne. At the very beginning of his researches he discovered the microbe responsible for it. It is a micro-bacillus somewhat resembling that of chicken-cholera, but finer, less visible, and differing greatly in physiological properties. It has no effect on hens, but kills rabbits and sheep. It is easily cultivated in a sterilized veal-broth. If an infinitesimal dose be inoculated into a pig, illness and death, with all the characteristics common to so-called spontaneous cases, promptly ensue.

Pasteur and Thuillier first made sure that rouget does not recur. They then succeeded in transforming it into virus-vaccine, a task which continues to present great difficulties, particularly by reason of the fact that there exist in France many different breeds of pigs, in which susceptibility to rouget varies very considerably.

In June, 1882, four young pigs from the department of Vaucluse, where swine-fever is endemic, were sent to the laboratory in the Rue d'Ulm to be vaccinated. In November they were returned to their native place, where swine-fever was still raging. Every possible means was taken to make them catch the disease: they were shut up in a stye with pigs suffering from it, infected matter was mixed with their food, and finally they were inoculated with the most active virus. They withstood all these tests, while two animals from the same litter were killed by inoculation with the same virus.

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[1] So called from the red blotches which it produces on the skin of animals suffering from it, known in England as swine-fever. [Trans.]

Pasteur had proved that "viruses are not morbid entities, and that they can affect the form and more particularly the multiple physiological properties of the media in which they live and multiply. In consequence, and in spite of the fact that it belongs to the species of living microscopic beings, virus is capable of modification. One can either reduce or increase it, and each of these conditions can be fixed by culture. A microbe is virulent in its effect on an animal when it is capable of multiplying in its body as a parasite, and by causing through its own reproduction diseases which result in illness and death. If the microbe has lived in one particular species of animal, that is to say, that at various stages it has left one individual of the species and entered another, without having been subject to any appreciable outside influence during its passage, one can imagine this parasite as having arrived at a sort of fixed state, which is the maximum for individuals of that species." It is thus that the anthrax bacteridium varies little in being transmitted from one sheep to another in the same district. "But the virulence of a virus which is not at its highest point can be essentially modified in its passage through a series of individuals of the same species."

To give attenuated anthrax virus increasingly progressive virulence and bring it up to a maximum virulence, it is sufficient to inoculate it into young animals, and then in succession to others of more and more advanced age. This raises the question whether a virus which has reached its maximum in one species can be modified by transmission to another.

In December, 1882, Pasteur decided to go with Thuillier to try vaccination on pigs in the canton of Bollène (Vaucluse), where a local veterinary surgeon named Maucuer had begged him to come and study the swine-fever, which was devastating the neighbourhood, on the spot. Soon after their arrival they learnt that the breeding of rabbits and pigeons had been almost abandoned in the district because both were constantly attacked by fatal epizootic diseases; and they were struck with the idea of trying to find out whether there were not some connection between these diseases and rouget. Their first discovery was that rouget kills rabbits and pigeons.

The inoculated pigeon dies in six or eight days, after having displayed symptoms similar to those of chicken-cholera. If a second pigeon is inoculated with the blood of the first, a third from the second, and so on, death ensues more and more rapidly, and it is demonstrated that "the blood of the last pigeons was much more virulent to pigs than any infection obtained from a pig which had died of so-called spontaneous rouget."

"The passage of the microbe through rabbits had quite different results. Infection taken from a pig which had died of rouget, or cultures from it, inoculated into rabbits, always made them ill, and was usually fatal. If rouget is inoculated from rabbit to rabbit, the microbe acclimatizes itself in the rabbit. All the animals die, and death occurs in a very few days. Cultures of the blood of these rabbits in sterilized media become progressively easier and more abundant. . . .

"If one inoculates pigs with the blood of the last rabbits and compares the result with that produced by the first, one observes that the virulence has diminished progressively in passing through the series of rabbits. Soon the blood of rabbits inoculated into pigs is no longer fatal, although it produces illness. After their recovery they are immune to fatal rouget."

On quitting Bollène, Pasteur had left a certain number of vaccinated pigs in the care of M. Maucuer, with the injunction on the part of their owners to keep them for at least a year, that is to say, beyond the time of the annual outbreak of the so-called spontaneous disease, which ceased during the cold season and reappeared in the summer months.

On September 4, 1883, M. Maucuer wrote that the disease was raging in his neighbourhood, but that "not a single vaccinated pig has died. At Saint-Blaise your vaccinated pigs are the only ones left alive . . . the mortality is so great that it has never been equalled." And on September 9th: "At M. de la Gardette's the non-vaccinated, without exception, to the number of seven, have been attacked, four are already dead, and the three others dying. The vaccinated are all flourishing."

Pasteur concluded that: "1st. Even the most violent epizootic rouget can be prevented by inoculations of attenuated virulent virus. 2nd. It is, moreover, proved that the duration of immunity exceeds one year, and that consequently this duration is ample for the requirements of pig breeding, since the fattening of these animals never lasts more than a year."

CHAPTER XXXIV

PUBLIC TRIBUTES

The farmers, who had been among the first to benefit by Pasteur's discoveries, wished to show their gratitude to him.

The Agricultural Society of Melun had a medal, bearing an effigy of Pasteur, struck to commemorate the experiments at Pouilly-le-Fort.

The town of Aubenas put up a statue to the famous agriculturist, Olivier de Serres, who first imported the mulberry-tree and started sericulture in France. They wished to include Pasteur, who had saved the industry, in the tribute paid to him who created it. At the invitation of the town he came to receive, amidst acclamations, a medal and a work of art which were presented to him.

Nîmes and Aurillac followed this example.

A number of scientists, friends, and admirers joined in offering Pasteur a medal commemorative of his discoveries. On June 25, 1882, J.-B. Dumas, Jamin, President of the Academy of Science, and several other representatives of the subscribers, went to Pasteur's abode in the École Normale. Dumas, who still carried lightly the weight of his eighty-two years, said, when presenting the medal, which was the work of Alphée Dubois :

" My dear Pasteur, forty years ago you entered this house as a pupil. From the beginning your masters foresaw that you would bring honour to it, but no one would have ventured to predict what brilliant services you were to render to science, to your native land, and to the world."

Dumas briefly recalled the discoveries of his former pupil, and ended thus :

" My dear Pasteur, your life has held nothing but success. The scientific method of which you make such unfailing use, owes to you its greatest triumphs. The École Normale is proud to count you among the number of its pupils, the Academy of Science boasts of your achievements ; France gives you a place among her glories.

" At the moment when tributes of public gratitude are being offered to you on all sides, the homage that we bring in the name of your friends and admirers, may appear to you worthy of special attention. It springs from a spontaneous and universal sentiment, and it preserves for posterity a faithful representation of your features.

" May you, my dear Pasteur, long live to enjoy your fame and to contemplate the ever richer and more numerous fruits of your work. Science, agriculture, industry, humanity, will be eternally grateful to you, and your name will live in their annals among the most illustrious and most venerated."

Pasteur listened with deep emotion to the sincere voice of this old man who had been the object of his earliest devotion, whom he still regarded as his master, and of whom he could only think with veneration. He replied by a few words of thanks.

" . . . What can I do henceforth ? Up till now praise has inflamed my ardour, and has only inspired me to make myself worthy of it by fresh efforts ; but that which you have just expressed in the name of the Academy and the learned societies, deprives me of courage."

When a national recompense was awarded to Pasteur in 1874, Paul Bert, who proposed the motion, remarked that the suggested pension was a very modest one compared with the services rendered. But, he added, your committee thinks " that the economic and hygienic results of M. Pasteur's discoveries will soon be so considerable that the French nation will think it just, later on, to increase the witness to its gratitude towards him and towards the science of which he is one of the most famous representatives."

These predictions were realized in 1883. Paul Bert had the satisfaction of proposing a new motion to raise Pasteur's pension to 25,000 francs, and he gave himself the pleasure of repeating a saying of the great physiologist Huxley at a meeting of the Royal Society in London: " Pasteur's discoveries have brought France more than the five milliards of indemnity paid to Germany after the war of 1870."

The town of Dôle had invited Pasteur to be present on July 14, 1883, at the placing of a commemorative tablet on the house in which he was born. As he stood before this humble building in the little Rue des Tanneurs, Pasteur expressed his thanks :

" Gentlemen, I am deeply touched by the honour which the town of Dôle has done me, but you must permit me, while expressing my gratitude, to protest against this excess of glory. In paying me a tribute, which is only rendered to the illustrious dead, you are encroaching prematurely on the judgment of posterity.

" Will it ratify your opinion, and would you not have been wiser, Monsieur le Maire, to warn the municipal council not to take such a hasty resolution ?

" After having protested, however, Gentlemen, against such a striking expression of an admiration which I do not deserve, allow me to say that I am touched and moved to the depths of my soul. Your sympathy has united on this commemorative tablet the two things which have been at the same time the passion and the joy of my life : love of science and love of home.

" Oh, my father and my mother ! Oh, my vanished dear ones who lived so modestly in this little house, it is to you that I owe everything ! Your enthusiasms, my brave mother, you passed on to me. If I have always associated the grandeur of science with that of my native land, it is because I was permeated with the sentiments with which you had inspired me. And you, my dear father, whose life was as rough as your work, you showed me what could be accomplished by untiring patience. It is to you that I owe indefatigableness in daily toil. You possessed not only those qualities of perseverance which make lives useful, but you also admired great men and great things. To look up, to learn from above, always to try and rise higher, that is what you taught me. . . .

"May you both be blessed, my dear parents, for what you were, and let me transfer to you the homage paid to-day to this house. . . ."

At the moment when he was invoking the memory of his father and mother, Pasteur could not restrain his tears, and his voice broke; his son was obliged to read the end of his speech.

CHAPTER XXXV

RABIES

OF all human maladies, rabies has one favourable peculiarity: though the most dreaded, it claims perhaps the fewest victims, and is, at any rate, the one from which it is easiest to protect oneself. It is unknown in Australia, where its entrance is prevented by the long period of quarantine required before imported dogs are admitted. In Germany strictly enforced police regulations have resulted in its almost complete disappearance. In France, however, such regulations have never obtained, and cases of rabies still occur.

Human rabies is, as a rule, caused by the bite of a mad dog. It does not appear in all those bitten, but when once it shows itself it is almost invariably fatal, so much so that many of these unhappy people consider themselves as condemned to the most horrible of deaths, and await with daily increasing anguish the uncertain hour of the beginning of their torture. This period of waiting may last ten, fifteen, or most often forty days, sometimes several months,—or even years, if one is to believe certain accounts which can, however, only be accepted with the greatest reserve. Death, inevitable as soon as the first symptoms have appeared, is sometimes easy though always pathetic by reason of its certainty, but often horrible. The impression of its horror haunts the imagination and is the only one retained by the memory. This was perhaps what determined Pasteur to attack the terrible disease, and to carry on, regardless of the immense strain, that struggle which was to last five years and end in a brilliant victory.

Two serious and unfortunately widespread errors play an important part in the spread of rabies:—people are misled by the common meaning of the word *rage* or madness, and imagine the mad dog in a state of fury and always ready to bite;—they also believe that dread of water is a constant symptom of the disease, so much so that rabies and hydrophobia are regarded as synonyms. Hence are drawn two conclusions dangerous by reason of the false security which they inspire,—that there is nothing to fear from a dog which appears quiet or from a dog that drinks.

Now hydrophobia is a symptom of human rabies, and is not observed in a mad dog, which drinks readily and without difficulty, and even, impelled by a raging thirst, with avidity up till the time when prevented doing so by the terminal paralysis.

Moreover an outbreak of fury is only one phase of the disease; it is not thus that rabies begins, and in some forms it never occurs.

The saliva in a dog incubating rabies may be virulent many days before there is any change in the animal's behaviour. The first change, and one at first not sufficiently marked to attract attention, is often an exaggerated display of affection, the dog becoming more than usually demonstrative. If this dog should lick a hand on which is even the slightest abrasion, so slight as to be unnoticed by the owner of the hand himself, it may transmit rabies and may disappear without anybody knowing what has become of it—this is no rare thing for a mad dog—and the victim will then be unable to give any account of the origin of the disease from which he is dying. It is also conceivable that virulent saliva falling on some object or other, may be touched by a careless or unsuspecting hand.

It is probable that the explanation of certain facts cited as examples of exceptionally prolonged incubation must be sought in occurrences of this nature. On November 2, 1874, in a small town in Algeria, a Sergeant Lechenet went to the assistance of one of the soldiers of his regiment who had been attacked by a mad dog. Both men were bitten. The non-commissioned officer had himself cauterized at once with a red-hot iron. The soldier was only cauterized on the following day, and died of rabies forty-eight days later. Lechenet died of the same disease on August 31, 1879, without being again bitten. These are the facts. They were reported to the Academy of Medicine as a case of rabies-incubation lasting nearly five years, but there does not seem sufficient justification for this conclusion. There is no proof that in the weeks preceding his death, Sergeant Lechenet had not incurred a fresh inoculation without being aware of it.

In December, 1880, Dr. Lannelongue informed Pasteur that a child was dying of rabies in one of his wards at the Sainte Eugénie Hospital. Pasteur took a little mucus from this child's mouth four hours after death, and after diluting it with water, inoculated two rabbits which both died in thirty-six hours.

Drs. Lannelongue and Maurice Raynaud made similar experiments themselves. They obtained the same results, and had no hesitation in coming to the conclusion that the rabbits had died of rabies.

Pasteur would not give a verdict so quickly, and continued his investigations. Saliva and blood from the first rabbits were inoculated into new animals, which died in less than thirty-six hours. An examination of the blood showed a micro-organism in the form of an 8 which can be cultivated in series in veal-broth; the virulence of this organism can be preserved in successive cultures; one can therefore state positively that it is the specific agent of the disease.

There is nothing characteristic about the shape of this organism, but in its reactions, and especially by the results obtained on inoculation into various animals, it resembles no known microbe.

In a note communicated to the Academies of Science and of Medicine, Pasteur cautiously announced "a new disease induced by the saliva of a child which had died of rabies," which was an exact statement of the experimental fact.

Following up the study of the new microbe, he found it in the saliva of children who had died of any disease, and even in the saliva of people in normal health; he shortly afterwards declared that the "new disease" had no connection with rabies; it differs not only in its symptoms, but still more in this important particular: it develops immediately on inoculation, without the intervening period of incubation which in rabies is never absent.

Two years later this microbe was rediscovered by Talamon and Fraenkel in the lungs of persons who had died of pneumonia; it has received the name of pneumococcus; it is a common organism which becomes pathogenic under certain conditions which are fortunately not always present together.

The saliva of animals infected with rabies is thus found capable of transmitting another disease. It was most important to seek elsewhere for the virus of rabies, and particularly in the nervous system, as this seemed from all the symptoms which had been observed to be the chief seat of the mischief.

Galtier, Professor at the Veterinary School of Lyons, wrote, however, to the Academy of Medicine in January, 1881, that he had inoculated, more than ten times unsuccessfully, "the product obtained by compression from the cerebral substance of the cerebellum and of the spinal cords of mad dogs."

Pasteur was more fortunate. On May 30, 1881, he announced in his own name and those of his collaborators, Chamberland and Roux, to the Academy of Science: "We have several times and often with success inoculated the *medulla oblongata* or spinal bulb and even the frontal portion of one of the hemispheres and the cerebro-spinal fluid. Under these conditions the rabies had an incubation period of normal duration.

But "it is a trial to an experimenter to be condemned to wait for whole months to see the result of one experiment when the subject entails a great many." Some method had to be found for shortening this time of delay.

The most minute researches had not served to discover the microbe of rabies. The central nervous system, so perfectly protected in the midst of the body, must form the principal site of its growth, and in order to take specimens absolutely guaranteed from contamination.

it seemed that one must deal with it as with ordinary cultures. The bulb of a mad dog was exposed and the surface of the organ first sterilized by burning; then with the drawn out end of a glass tube, a small piece of nerve was sucked out from the deep part; this substance, pounded or dissolved in a little water or broth, could be injected with a Pravaz syringe; all these operations being performed, be it clearly understood, with the most meticulous aseptic precautions. The only thing remaining is to transport the virulent material beneath the dura-mater in contact with the brain.

"As a rule," writes Dr. Roux, "an experiment once thought of and discussed was started without delay. This one, from which we hoped much, was not immediately carried out. Pasteur, who was forced to sacrifice so many animals in the course of his beneficent studies, had an absolute horror of vivisection. He assisted at a simple operation, such as a subcutaneous inoculation, without much distress, but even then if the animal made a little sound, Pasteur was filled with pity and lavished upon the victim words of comfort and encouragement which would have been ludicrous if they had not been touching. The idea of making a hole in a dog's skull troubled him. He was very anxious for the experiment to be completed, but he was afraid of seeing it performed. I did it one day when he was away. The next day when I informed him that the intracranial operation presented no difficulty, he was full of pity for the dog. 'Poor beast, its brain is no doubt injured, it must be paralysed.' Without answering I went down to the basement to fetch the animal, and brought it into the laboratory. Pasteur was not fond of dogs, but when he saw this one, as lively as possible, and poking about inquisitively everywhere, he expressed the greatest satisfaction, and lavished kind words upon it. He was infinitely grateful to this dog for having stood the trephining so well, and so having abolished any scruples he might have had about trephining in the future."

This dog was attacked with rabies fourteen days after inoculation.

The virus exists in the brain, in the bulb, the whole cord, and the nerves; rabies can be transmitted with pieces of the pneumo-gastric and the sciatic.

Pasteur made all these researches with the idea constantly in mind of attenuating the virus and establishing a method of prophylaxis.

This result had been obtained for chicken-cholera, anthrax, and swine-fever. Animals vaccinated against these diseases were no longer liable to contagion. But there could be no question of preventive vaccination in human beings against rabies, for who would submit to it? The chances of being bitten by a mad dog are too remote. What was needed was a means of vaccination after the bite, but the hitherto universally accepted medical teaching considered this as an absolute impossibility.

It was a dogma, undisputed since Hippocrates and now accepted as an axiom, that viruses, once having entered into the human body, became inaccessible. One could avoid infection with variola, but from the moment when variola-virus was introduced into the organism, nothing could arrest its further development. One could destroy the virus of rabies by immediate cauterization of the bitten flesh, but if the virus escaped the action of the hot iron, medicine was powerless; and every doctor knew how often even the quickest, most drastic, and apparently most thorough cauterization had failed to prevent the development of rabies.

Fortunately Pasteur recognized no dogma in experimental matters: experiment would decide whether his hopes were vain.

On February 25, 1884, he announced to the Academy of Science that "the passage of rabies-virus through different species of animals allows of a modification of the virulence of the virus, to a greater or less extent. Rabbits, guinea-pigs, hens and monkeys take rabies. When after successive passages, the virus has arrived at a state of fixation in relation to the species, its virulence is far from being unchanged, and is markedly different from that of canine rabies of a virulence fixed by numerous passages from dog to dog from time immemorial."

On May 19, 1884, Pasteur completed these communications: The virulence of rabies virus is increased when transmitted from a dog to a rabbit, and then from rabbit to rabbit; at the same time the length of the incubation period decreases even to as short a time as seven days. On the contrary "on passage from dog to monkey, and afterwards from monkey to monkey, the virulence of rabies-virus is decreased at each passage. If when the virulence has been diminished by these passages from monkey to monkey, it is returned to a dog or to a guinea-pig, it remains attenuated. In other words, the virulence does not revert with a leap to the virulence of that of the ordinary mad dog of the street. Under these conditions, the attenuation can easily be increased by a small number of passages from monkey to monkey up to a point when it will no longer produce rabies in a dog except by hypodermic injection. Even inoculation by trephining, infallible method though it be for transmitting rabies, may fail to produce a result, though nevertheless making the animal refractory to rabies.

"Thanks to the length of the time of incubation of rabies following bites, I have every reason to believe that a refractory state may be established in those who have been bitten, before a mortal disease declares itself."

This method of attenuation is, however, not a very practical one. It does not give absolute security. It is only applicable as long as an unlimited number of monkeys is available. Could not the action of oxygen, which had already served to attenuate the virulence of cultures of fowl-cholera and anthrax bacteridia, be utilized? After many attempts success was achieved, and Pasteur could draw up the proclamation of victory which he read to the Academy of Science and to the Academy of Medicine on October 26 and 27, 1885, under the modest title: *Method of Preventing Rabies after a Bite.*

"After experiments which may be described as numberless, I have arrived at a practical and prompt method of prophylaxis, the successes of which on dogs are already so numerous and certain that I am confident that it is generally applicable to all animals and even to man himself."

By a series of ninety passages from rabbit to rabbit, Pasteur had obtained a virus which produced rabies after a seven days' period of incubation, and this interval showed hardly any tendency to further reduction after more numerous passages. "As a result of this, nothing is easier than to have constantly available, over long periods of time, a rabies-virus absolutely pure and almost if not quite invariable. There lies the practical problem of the question.

"The cords of rabbits contain rabies-virus with a fixed virulence throughout their entire length.

"If lengths of some centimetres of cord are cut off, every possible precaution being taken against contamination, and suspended in dry air, the virulence slowly decreases in the cord, up to complete disappearance. The time taken for extinction of the virulence varies a little with the thickness of the bits of cord, and more particularly with the outside temperature. The lower the temperature, the longer is the virulence preserved. These results give the scientific side of the method.[1]

"These facts being established, I will describe the method of immunizing a dog to rabies in a relatively short time.

"In a series of flasks in which the air is kept dry by pieces of potash placed on the bottoms, one hangs each day a piece of fresh rabies cord from a rabbit which has died of rabies developed after seven days' incubation. Every day one inoculates hypodermically into the dog a Pravaz syringeful of sterilized broth, in which an emulsion of a small piece of one of the dried cords has been made, beginning with a cord removed long enough before to ensure its substance being no longer virulent. Previous experiments have served for this determination.

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[1] "If the rabies cord is protected from air in carbonic acid gas in a moist state, the virulence is preserved (at least for many months) without variation of its rabies-inducing intensity, so long as it is protected from the changes due to foreign microbes." (Note by Pasteur.)

On the following days one repeats the performance with cords removed at intervals shorter by two days each, until a very virulent cord, which has only been placed in a flask for one or two days, is reached.

"The dog is now refractory to rabies. He can be inoculated subcutaneously with rabies-virus, or even on the surface of the brain by trephining, without rabies showing itself.

"By applying this method, I had obtained fifty dogs of all ages and breeds immune to rabies, without a single failure, when there arrived, quite unexpectedly, at my laboratory three people from Alsace:

"Théodore Vone, a retail grocer of Meissengott, near Schlestadt, bitten in the arm, on July 4th, by his own dog, which had gone mad.

"Joseph Meister, aged nine, also bitten on July 4th, at eight o'clock in the morning, by the same dog. This child, knocked down by the dog, had a number of bites on the hand, legs and thighs, some of them so deep as to make even walking difficult. The largest of these bites had been cauterized with carbolic acid only twelve hours after the accident. . . .

"The third person, who had not been bitten, was the mother of little Joseph Meister.

"At the autopsy of the dog, killed by his master, the stomach was found to be full of hay, straw and bits of wood. The dog had been furiously mad. Joseph Meister had been taken from under him covered with saliva and blood.

"M. Vone had severe contusions on his arms, but was quite sure that his shirt had not been pierced by the dog's teeth. As there was no reason to be anxious about him, I told him that he could return to Alsace that same day, which he did; but I kept little Meister and his mother with me.

The weekly meeting of the Academy of Science took place precisely on July 6th; I saw there our confrère Dr. Vulpian, to whom I related what had happened. Dr. Vulpian and also Dr. Grancher, Professor of the Faculty of Medicine, were kind enough to come at once to see little Joseph Meister, and note his condition and the number of his wounds. There were no less than fourteen of them.

" The opinion of our learned colleague and of Dr. Grancher was that, owing to the number and severity of the bites, Joseph Meister was almost inevitably certain to develop rabies. . . .

" The death of this child seeming unavoidable, I decided, not without deep and cruel anxiety, as one may well imagine, to test on Joseph Meister the method which had been constantly successful on dogs. . . .

" Consequently, on July 6th, at eight o'clock in the evening, sixty hours after the bites of July 4th, and in the presence of Drs. Vulpian and Grancher, he was inoculated under the skin of the right hypochondrium with a half syringeful of the cord of a rabbit which had died on June 21st, kept since then, that is for fifteen days, in a flask of dry air.

" On the following days, fresh inoculations were made, always in the hypochondrium " and of the same dose.

" On July 7th, at nine in the morning, the child received an injection of a half syringe of fourteen day cord ; again on July 7th at six o'clock in the evening, the same quantity of twelve day cord.

" On July 8th, at the same hours, two injections of cord of eleven and nine days.

" On July 9th, at eleven o'clock in the morning, a single injection of eight day cord. From this date onwards, a single injection was made, at eleven o'clock, of cord one day more recent than that of the day before, with the result that on July 16th Joseph Meister received a thirteenth and final injection of a cord one day old.

" Each of the cords used was inoculated into two fresh rabbits ' so as to trace the state of virulence of these cords.' The cords from fifteen to seven days, used July 6th to 10th, not being virulent, the rabbits did not develop rabies. The other cords all showed themselves more or less virulent. That of July 11th (six days) gave rabies after eight days' incubation ; those of July 15th and 16th (two days and one day), after seven days' incubation.

"During the last days, I had therefore, inoculated Joseph Meister with the most virulent rabies-virus, that of a dog reinforced by passages from rabbit to rabbit, a virus which gives rabies to these animals after seven days' incubation, to dogs after eight or ten.

"When the immune state is reached, one can without causing any inconvenience, inoculate the most virulent virus in any quantity. It has always seemed to me that this has no other effect than that of fixing more firmly the refractory state to rabies.

"Joseph Meister has therefore escaped not only the rabies which his bites might have produced, but also that which I had inoculated to test the immunity due to treatment, a rabies more virulent than that of ordinary mad dogs.

"The final very virulent inoculation has another advantage in limiting the duration of the fears that one may have of the consequences of bites. If rabies could appear, it would show itself sooner after a virus more virulent than that of the bites. When August came I confidently predicted the future condition of Joseph Meister. Now to-day, three months and three weeks after the date of the accident, his health leaves nothing to be desired."

It would be enough to cut out one line of this communication in order to give it the frigidity of an official report. Pasteur says nothing of the fears which assailed him when he made the last inoculations, those *capable of giving rabies.* The studies he had pursued for five years, the innumerable experiments carried out so methodically, the opinion expressed by two eminent doctors who were acquainted with the experiments and had observed the results, all this entitled him to act boldly; canine and human rabies do not present the same symptoms, but from the physiological point of view they do not differ. . . . Pasteur said all this to himself, but nothing could prevent his experiencing the most poignant anxiety when he had to turn from the dog to the human being. The thought that Joseph Meister owed his life to him was a recompense which his brave heart deserved.

In October, the Mayor of Villers-Farlay (Jura) gave Pasteur another opportunity of applying his method. A young shepherd, Jean-Baptiste Jupille, hardly fifteen years old, was watching his flock with six small comrades playing round him: a big dog, with bristling coat, wild eye, and gaping jaws fouled with dust and saliva, suddenly appeared and fell upon them. Jupille, wishing to protect the children, went straight for the dog, struggled with and mastered him, muzzled him with the lash of his whip, and beat him to death with his sabot. He received deep wounds on both hands.

The autopsy proved that the dog was mad. Joseph Meister's treatment had been begun sixty hours after the infliction of the bites. Jupille only reached the laboratory at the end of six days, but nevertheless he was cured.

In his communication of October 26, 1885, to the Academy of Science, Pasteur had only been able to allude briefly to this new case, the treatment of which had only just been begun. Vulpian, who had encouraged and followed his first attempt, asked permission to express the sentiments of admiration with which Pasteur's words had inspired him: "These sentiments," he said, "will, I am sure, be shared by the whole medical profession.

"Rabies, that terrible disease against which all attempts at treatment have hitherto failed, has at last found a remedy! M. Pasteur, who has had in this line no predecessor but himself, has been led by a series of researches, pursued for years without interruption, to the creation of a method of treatment, by means of which the development of rabies in a man recently bitten by a mad dog can be prevented with certainty. I say 'with certainty' because, after what I have seen in M. Pasteur's laboratory, I have no doubt of the unfailing success of this treatment when carried out practically and thoroughly a few days after the bite of a mad animal.

"A regular centre for the treatment of rabies according to M. Pasteur's method ought to be organized immediately. It is essential that every person bitten by a mad dog should be able to benefit by this great discovery, which puts the seal upon our illustrious colleague's fame, and will bring great glory to our native land."

As soon as the results obtained in these two first successful attempts, on Joseph Meister and Jupille, were known, many people came to ask for the same treatment. By February 28, 1886, the number of patients who had undergone preventive inoculations had already reached three hundred and five.

Pasteur was astonished that such a total should have been reached so quickly, but he soon discovered the reason. While rabies was regarded as incurable, everybody endeavoured to reassure those who had been bitten; they declared that the dog was not mad even when a veterinary-surgeon or a doctor had reported to the contrary, and often where death had ensued meningitis was certified as the cause to avoid the mention of rabies.

Very careful statistics were compiled of all cases treated in the laboratory. Pasteur required a certificate given by a doctor or a veterinary-surgeon that the dog was mad. Whenever possible the rabies in the dog was confirmed in the laboratory itself by the inoculation of nerve-tissue taken from the dead animal into rabbits and guinea-pigs. Among the first cases was that of a man named Lordé, aged thirty-six, living at Lasse (Basses-Pyrenees), who was bitten on October 25, 1885, and arrived at the laboratory on November 21st, twenty-seven days after the bite. The same dog had bitten seven pigs and two cows on the same day. These animals had died of rabies. Incubation was short in the pigs,—from a fortnight to three weeks; longer in the cows,—thirty-four and fifty-two days; it must be noted that immediately after having been bitten, the cows had been deeply cauterized with a red-hot iron. It was after the death of the pigs that Lordé took fright and set out for Paris. The treatment was absolutely successful.

The first case in which treatment proved ineffectual was that of Louise Pelletier, aged ten, bitten on October 3rd, and not brought to the laboratory till

November 9th, thirty-seven days later. She had deep wounds on the head and in the arm-pit. That on the head still measured twelve to fifteen centimetres on the day of her arrival. "This wound," says Pasteur, "caused me grave anxiety. I begged Dr. Vulpian to come and examine it. In the scientific interest of the method, I ought to have refused to treat a child who had arrived so late and in such a serious condition, but from humane motives and in view of the parents' distress, I should have reproached myself if I had not tried everything."

Rabies declared itself eleven days after the end of the treatment. One might ask, and some malicious people did ask, whether it was due to the dog bite, or to the inoculations. The harmlessness of the latter, already tested on so many bitten people of all ages, could be affirmed without question, but Pasteur was not content with a moral certainty when he could rely on an experimental test. The virus of a dog affected with ordinary rabies, inoculated by trephining into a rabbit, gives rabies in fifteen to eighteen days. The exalted virus used in treatment gives rabies to the rabbit after only seven days' incubation. Pasteur asked and obtained leave to remove a little cerebral matter from the young Pelletier: the rabbits inoculated with it developed rabies after eighteen days, which proved that death was due to the dog's bite.

On March 1, 1886, Pasteur drew the attention of the Academy of Science to the evidence furnished by his latest statistics. Bouley had estimated, towards the end of the Empire, that the mortality after bites from mad dogs was forty per cent. Leblanc, chief of the Sanitary Police, investigating another period, found a mortality of sixteen per cent. Quite recently out of five persons bitten near Paulin, five had died. Taking the lowest figures, those of Leblanc, out of the three hundred and fifty people treated in the laboratory, one would have expected a mortality of fifty-six; there had been one only, and that one known to have been very seriously bitten and treated very late. Pasteur was able to say at the end of his communication:

"It is obvious, relying on the strictest statistics, what a large number of people have already been rescued from death.

"Prophylaxis against rabies is established.

"The establishment of an institution for vaccination against rabies had been justified."

The Academy of Science nominated a committee with the object of finding means to create such an establishment. The first decision was to open a subscription list in France and abroad.

At first those bitten had been treated in the laboratory in the Rue d'Ulm. They were lodged more or less comfortably in the neighbouring hotels, and in the court-yard of the École Normale was constantly to be seen a picturesque procession, resembling a pilgrimage to some miraculous shrine, of people from all countries, With an ever-increasing crowd, however, it became necessary to make other arrangements.

In this month of March, 1886, nineteen Russians from Smolensk presented themselves at the laboratory. They had been attacked a fortnight before by a mad wolf. All had been cruelly bitten, and five had such serious wounds that they had to be taken to the nearest hospital. One of these died under treatment, two others some days after the treatment was finished. Pasteur was terribly upset, and asked himself anxiously what would become of the sixteen survivors. He decided, in conjunction with Dr. Grancher, who had taken charge of the inoculations, to recommence the treatment once or twice, going as far as the freshest cords. The sixteen Russians were cured.

Pasteur learnt at this time, through different communications made to him, that out of fifty-two cases observed in France, distributed over a long period, the mortality from the bites of mad wolves was as high as eighty-two per cent. In Russia everyone bitten by a mad wolf was regarded as condemned to death. This special gravity is due, not to the nature of the virus, as was determined by experiments made in the laboratory, but to the number, depth, and position of bites from a wolf, which attacks especially the head and face, and is infuriated with the victim.

Pasteur resolved to modify his method in order to make it more efficacious in wounds of a serious nature or those inflicted long before. Being as always anxious to rely on experimental findings, he tried to produce the refractory state in dogs by commencing treatment only after they had been inoculated intercranially with ordinary rabies-virus. The disease so inoculated invariably breaks out after fourteen or fifteen days' incubation; to accelerate matters by using the exalted virus in its different degrees of attenuation, it is necessary to begin vaccination without too much delay, that is, on the very next day after intercranial inoculation, and "the series of protective cords must be given within twenty-four hours, or even during a shorter period, and the treatment must then be repeated every two hours, once or twice." By proceeding thus, the dog is protected from rabies, and is rendered refractory.

Encouraged by the results obtained on the Russians from Smolensk and by his new experiments, Pasteur modified his method by making it more rapid and powerful in all cases, and still more rapid and drastic in the case of bites on the face and of multiple and deep wounds on other bare parts of the body. During the first three days, he carried out a complete treatment, passing from a twelve day cord to one of a single day. During the next three days a fresh treatment from an eight to a one day cord; and during the following four days, a third and last treatment from a four day cord to one of one day.

Pasteur adds: "If the bites are not healed and if the persons bitten have delayed coming for treatment, we sometimes, after an interval of one or two days' rest, recommence the same treatments and carry them on for periods of four to five weeks, which are the dangerous times for children bitten on the face."

Out of seventeen hundred and twenty-six French people who came to the laboratory of the École Normale before November 1, 1886, the treatment was inefficacious in only twelve cases, including the unfortunate Louise Pelletier and Moerman who arrived much too late, namely, thirty-seven and forth-three days after having been bitten. The mortality, instead of reaching the figure of sixteen per cent. indicated by Leblanc, which would have given two hundred and seventy-six deaths, was not even one in a hundred and seventy. This represents at least two hundred and sixty-four people saved from rabies.

As Pasteur remarked, it could be affirmed that among French people bitten during that year, 1885–1886, very few did not come to the laboratory, and nevertheless of this small minority seventeen cases of death from rabies were known. One of these was particularly instructive, that of a man of the Sarthe who was stricken with rabies forty-two days after being bitten. Three other people bitten at the same time, by the same dog, hurried to the laboratory; only one, Moerman, succumbed.

Statistics are only of value when applied to large numbers. By considering this imposing total of seventeen hundred and twenty-six people treated, one can affirm, with a near approach to certainty, that among these people at least sixteen per cent. would have been attacked by rabies and would have died. But if one is content to take a single particular case all certainty disappears. Vulpain and Grancher had formed the opinion that "owing to the severity and number of his bites, Joseph Meister was almost inevitably certain to develop rabies." This *almost*, however, signified that in their opinion the injured child had still some chance of being cured.

During this year, 1886, the doctors convinced *a priori* that the virus once within the body could not be destroyed, declared that Joseph Meister and many others had been cured because they would naturally have recovered, since for various reasons they had escaped invasion by the rabies-virus; this virus may have been washed away by the blood flowing from the wound, or have been destroyed by well performed cauterization. . . . The vaccinations had had nothing to do with the cure; all that could be said of them was that they had not been harmful, but after the deaths of Louise Pelletier and the three Russians from Smolensk, and the inauguration of the intensive method, the treatment was denounced as dangerous. Some fanatical opponents treated Pasteur as an assassin.

Up to this time little had been known about human rabies. Many doctors had never seen it. The descriptions given in the classic works were inadequate and incomplete, and because the symptoms observed in some cases of unsuccessful vaccination did not resemble in every detail these unfaithful pictures, Pasteur was accused of transmitting to man a new variety of rabies, that of the rabbit. The evidence obtained by the inoculation of the cerebral substance taken from Louise Pelletier was regarded as of no value. If the child had died as a result of the treatment, the material should, like vaccine cord, have given rabies after seven days incubation; as the incubation had lasted twenty-eight days, it was proved to be a case of canine and not rabbit rabies. This, however, was disdainfully described as a laboratory experiment which had no clinical value.

These polemics were moreover not confined within the bounds of Academies or scientific reviews, they spread to political journals and to general conversation: there were Pasteur enthusiasts but also violent anti-Pasteurites. A Hungarian woman presented herself in the Rue d'Ulm and gave the date on which she had been bitten. She had been in Paris six days. When asked why she had delayed coming, she answered: " I have read and heard such alarming accounts of your methods and results, that I have lost confidence. I am frightened."

People who had been bitten and were being treated in the Rue d'Ulm, did not lose their right to die of common diseases. When one of these cases became known, there was a rush to the laboratory, and if the information given by the doctor in charge, or by the family, could possibly be given such an interpretation, the treatment was accused of being responsible. The feelings of some were so strong, that they urged parents to take judical proceedings for manslaughter due to negligence.

Fortunately Pasteur, whose health had suffered from so much work and fatigue, had been obliged to go to the south for a rest and was at Bordighera, where a friend had offered him hospitality. He did not hear directly of all these altercations. But even there he received anonymous letters, full of abuse and threats. These attacks wounded him deeply. He said sadly one day: "I did not think I had so many enemies." He had, however, an even greater number of friends and admirers who successfully defended him in his absence.

At the Academy of Medicine, Vulpian challenged one of the most ferocious opponents of Pasteur's system "What does our colleague want? Is it to prevent all those bitten by mad dogs or dogs suspected of being mad from having recourse to M. Pasteur's treatment? If so, what a responsibility he is assuming! If he succeeds in destroying the confidence which such success has inspired in doctors and persons injured by rabid animals, how many deaths will he not have to reproach himself with?

"Let him abandon this unjustifiable warfare. It thoughtlessly attacks one of the greatest discoveries ever made. The series of researches which have led M. Pasteur to this discovery are in every way admirable. Thanks to M. Pasteur, this terrible disease of rabies, which was a typically incurable malady, can be prevented or controlled with almost absolute certainty.

"Thus yet another service has been added to all those which our illustrious Pasteur has already rendered to humanity. The glory which his work has reflected on our country is beyond compare and keeps French science in the foremost rank. . . .

"The fame of M. Pasteur is such that it will resist any number of attacks. When the names and the work of the rest of us have been long covered by the rising tide of oblivion, the name and work of M. Pasteur will still be resplendent on heights far above the reach of those sad waves."

The English government had judged it expedient to have the results obtained in France officially verified. A commission was appointed, which was presided over by Sir James Paget, numbered among its members Sir John Lister, and had Victor Horsley as its energetic and devoted secretary. They came to Paris on April 12, 1886, worked for fourteen months, repeated all the essential experiments, and examined eighty-six people whose names had been taken from the registers of the laboratory of the Rue d'Ulm. There verdict was that "it may be taken as certain that M. Pasteur has discovered a method of preventing rabies comparable to that of vaccination for small-pox. It would be difficult to exaggerate the importance of this discovery, both as regards its practical application and its effect on general pathology."

This impartial testimony, given by men of science who had taken the trouble to study the question, must have consoled Pasteur for the malicious attacks with which the envious had not ceased to pursue him: he could, as advised by one of his colleagues in the Academy of Medicine, carry on his life's work without letting himself be disturbed by obscure blasphemers.

On December 27, 1886, the Academy of Science, awarded to Pasteur the Jean Reynard Prize after hearing Vulpian read the report, in which he declared Pasteur's work on rabies to be "one of the most magnificent in the records of science."

The subscription list opened to raise funds for the founding of an establishment for anti-rabies inoculation, to be called the Pasteur Institute, had brought in fcs. 2,586,680. The Emperor of Brazil and the Sultan of Turkey were among the subscribers, and the Czar had celebrated the return of the Russians of Smolensk by a gift of "truly imperial" magnificence.

A site of eleven thousand square metres was acquired in the Rue Dutot. The architect refused to accept a fee, the builders would only take out of pocket expenses, and the workmen laboured with unfailing good will.

On November 14, 1888, the Institute was opened in the presence of M. Carnot, President of the Republic. Pasteur said that there was not a stone in this noble building which did not represent a generous thought. He entered into possession with his health ruined, and to use his own rather melancholy expression, as a man "vanquished by time," but with the great joy of being assured that his work would survive him and continue and multiply the benefits it conferred.

In a speech made at this opening ceremony, Pasteur wished to give to his collaborators as a final word of advice the rule which he had always obeyed in his scientific work.

He recommended them to preserve that first enthusiasm inspired by bacteriology, that science born but yesterday, but born fully armed, which "has acquired such might from its recent conquests that it has captivated the minds of all." And he added: "Always accompany this enthusiasm with rigid restraint. Put forward nothing which cannot be proved simply and decisively.

"Cultivate the critical faculty. By itself it is neither an originator of ideas nor a stimulus to great things, but without it nothing is sound. It always has the last word. What I ask of you, and what you should ask of the disciples that you will make in the future, is the most difficult thing there is for the discoverer.

"To believe that one has made an important scientific discovery; to be in a fever to announce it, and to restrain oneself; for days, weeks, and sometimes years to fight against oneself; to force oneself to confute one's own experiments; and only to proclaim a discovery when all contradictory hypotheses have been disproved;—yes, this is an arduous task.

"But when, after very many attempts, one has at last arrived at certainty, one experiences one of the greatest joys the human mind can feel, and the thought that one will add to one's country's glory, makes this joy greater still."

CHAPTER XXXVI

PASTEUR IN HIS LABORATORY

PASTEUR could not leave without regret the house in the Rue d'Ulm, where he had spent so many happy years rich in discoveries. His collaborator, Émile Roux, has described,[1] in pages worthy of the most careful preservation, the life of this dear laboratory :

" . . . These studies on anthrax, the attenuation of virus, *rouget* in pigs, and rabies, had been accomplished by Pasteur in less than ten years, between 1876 and 1885, with aid of only a few collaborators, first M. Joubert, and later MM. Chamberland, Thuillier and Roux. The years spent in the laboratory of the Rue d'Ulm during this period of discoveries remain in my memory as the best of my life. To be near their work, both master and pupils lived in the École Normale. Pasteur was always the first to arrive ; every morning I heard his hurried and rather dragging step shake a loose stone of the pavement outside the window of the room which I occupied at one end of the laboratory. Hardly had he entered when, with a small card and a pencil in his hand, he went to the incubator to note the state of the cultures and descended to the basement to inspect the animals under experiment. Then we made autopsies, cultures and microscopic examinations. One must have actually seen Pasteur at his microscope to form any idea of the patience with which he examined a preparation. He looked in fact at everything with the same meticulous care, nothing escaped his short-sighted eyes, and we used to say as a joke that he saw the microbes growing in the broth. After this Pasteur wrote down what had just been observed. He did not allow anybody else to keep the records of the experiments. . . .

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[1] É. Roux, Sub-Director of the Pasteur Institute, *Pasteur's Medical Work*, in the *Chemist's Agenda*, 1896.

" A little before noon Pasteur was called to lunch; at half-past twelve he came down to the laboratory, and on our return we generally found him motionless before a cage, untiring in his observation of an interesting rabbit or guinea-pig. Towards two o'clock Mme Pasteur sent to fetch him, otherwise he would have forgotten to go to the various Academies and Committees of which he was a member. . . .

" Pasteur returned about five o'clock, and immediately informed himself of all that had been done, and took notes; memorandum-book in hand, he went to verify the labels stuck on the cages, then he told us about any interesting communications which he had heard at the Academy, and talked about the work on which we were engaged. It was at this moment that Pasteur became most expansive, especially if one drew him out by objections; then his clear eye became even brighter; his speech, which was rather slow to begin with, became gradually more animated and persuasive. He developed the most abstruse and startling ideas, he suggested the most daring experiments. This strict experimenter had a powerful imagination; to him nothing was absurd *a priori*. But his wildest flights always led to an experiment to be performed, and in the end he only held to what had been proved by it. His enthusiasm was so infectious that after having listened to him we were all full of plans for experiments. When we got him on to the subject of his first studies, he held forth most poetically about molecular dyssymmetry and its relation to the dyssymmetrical forces of nature. On those days Pasteur forgot the dinner-hour; Mme Pasteur had to send two or three times or come herself to fetch him, then he went off laughing and saying to us: ' It is your fault that I am in for a scolding.'

" The Laboratory was kept carefully closed; one could only get in by ringing at the main door which was always kept shut. Visitors never got beyond the hall; when M. Pasteur was working he did not welcome the arrival even of his friends; to interrupt him was to make him miserable. I can see him turning towards the intruder, waving his hand as if to send him away, and saying in a desperate and imploring tone: 'No, not now, I am too busy!' He was in reality the most simple and approachable of men, but he could not understand how anyone could disturb a scientist who was recording laboratory notes. When Chamberland and I were occupied with an interesting experiment, he would mount guard beside us, seeing from afar through the glass door any comrades who came to enquire for us, and going himself to meet them and head them off. These whims of Pasteur showed so naïvely that that his whole interest lay in work that they offended nobody.

"Pasteur has been reproached for not having thrown open his laboratory to pupils, who would have spread his ideas and his methods; it has even been said that he liked to keep his experimental procedures secret. Nothing could be more unjust; in his communications Pasteur has scattered the seed of his new ideas broadcast, and it is open to anybody to profit by them. He was indeed an incomparable teacher, putting forward no fact without giving all the information necessary to verify it. . . .

"Pasteur could only work comfortably in silence and meditation; he allowed no one near him but his collaborators—the presence of a single stranger was enough to distract him. One day when we went to see Wurtz at the School of Medicine, we found the great chemist in the midst of his pupils and the whole laboratory humming like a bee-hive. 'What,' cried Pasteur, 'you can work in the middle of this turmoil?' 'It stimulates ideas,' replied Wurtz. 'It would drive all mine away,' said Pasteur.

"Pasteur was always thinking out experiments; he put down his ideas in a little note-book or on small cards, which he carefully preserved. His left hand being helpless after the attack of paralysis in 1868, he left the carrying out of these experiments to his assistants; being a faultless experimenter himself, others found him very hard to please. For him there was no such thing as an impossible experiment; if we remarked that what he wanted done presented special difficulties he would say: 'That is your affair, see that it is done, and well done.' And he always made sure that it *was* well done—he distinguished between the good and the bad in it with admirable sagacity.

"A communication from Pasteur to the Academy of Science or to the Academy of Medicine was an event; this was because he published nothing incomplete. Each of his notes only filled a few pages of the reports, but it contained the substance of hundreds of experiments. Moreover, one can read and re-read them; one will always find something to take away; often a mere phrase points out a new path, and these are often such as are still untrodden. The whole Pasteur may be found in his writings; his imagination is revealed there by the depth and boldness of his generalizations, the accuracy of his mind in the justice of his views and the stability of his conclusions, his enthusiasm in the emotional language he uses.

"Before writing, Pasteur read and re-read the notes on the experiments, then he dictated to one or other of us, most often to Mme Pasteur. He kept the manuscript sometimes for weeks, constantly revising it; when he was satisfied, he made it known to us all, and discussed the expressions he had used with us; often he received comments impatiently, but he always took them into account when they were justified. . . . During this work of revision, the question which was under discussion developed strangely, and we, the collaborators of the master, who knew exactly at what point the experiments had left it, were often astonished to see how it had grown and changed in the note which was finally published.

" . . . Pasteur's passion for science sometimes led him into very amusing outbreaks. To him a man who could make a bad experiment was capable of anything. One day in the laboratory, when he was reading to us a work which seemed to him particularly bad, he cried out in exasperation: 'I shouldn't be at all surprised if the man who could write such stuff beats his wife!' As if wife-beating were the acme of scientific irregularity.

"Pasteur's great power lay in the fact that he was able to keep his thoughts concentrated without fatigue on one object. He followed out his idea without letting himself be distracted, and obtained everything possible from it; thus from a conversation with people who knew nothing at all about science, he would get something which would be useful to him in his researches. Of him one may also say that he made his discoveries by constantly reflecting on them. His thought attached itself stubbornly to difficulties and ended by solving them, as the intense flame of the blow-pipe continually directed upon a refractory body ends by melting it.

"At times when he was thus much pre-occupied, Pasteur remained silent even when with his family. Nothing could smooth out the lines on his brow until the solution was found. Then his face lit up, and this uncommunicative man let his joy overflow all around him, explaining what he had discovered and what he hoped to accomplish through it, for Pasteur's relatives were all associated with his scientific life; they felt the weight of his pre-occupation and shared in his relief. One could form no picture of Pasteur's career without knowing his family, especially Mme Pasteur. From the very beginning of their life together, Mme Pasteur grasped what sort of man she had married, and set herself to save him from all domestic worry, taking upon herself all household cares so that his mind might be perfectly free to devote itself to his researches. Mme Pasteur loved her husband up to the point of understanding his work. In the evening she wrote at his dictation and called forth explanations, for she was really interested in hemihedral facets and attenuated virus. She also realized that ideas become clearer when one has to put them into words, and that nothing suggests new experiments so well as describing those which have just been made. Mme Pasteur was not only an incomparable companion to Pasteur, but his best collaborator."

CHAPTER XXXVII

PASTEUR'S JUBILEE—LAST DAYS

In 1884 Pasteur had represented France at the International Medical Congress held at Copenhagen. He had been the object of enthusiastic demonstrations. He reckoned many admirers among the Danes, one of the most notable being the brewer Jacobsen, distinguished as much for his love of science as for his wealth, who had asked leave to have a bust of Pasteur executed in marble by Paul Dubois, in order to install it in the place of honour in his laboratory at Carlsberg.

In May, 1892, a committee was formed in Denmark to celebrate, on December 27th, Pasteur's seventieth birthday. This committee, "composed of scientists and disciples, who in their researches or their business had drawn inspiration from Pasteur's doctrines, decided to open a national fund in order to have a great commemorative medal struck."[1]

From Denmark the movement spread to Norway, and thence to Sweden, where the king headed the list of subscribers, and finally to France. In November the sections of Medicine and Surgery in the Academy of Science formed a committee for raising subscriptions towards "offering a remembrance and a tribute to their illustrious compatriot on the occasion of his jubilee."

On December 27, 1892, a crowd filled the great amphitheatre of the Sorbonne: members of the Institute, professors of faculties, delegates from foreign academies and learned societies, delegates from all the big schools, and lastly, in vast masses, hundreds of students.

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[1] Anonymous, Jubilee of M. Pasteur, in 4°, Paris, Gauthier-Villars, 1893, p. 1.

"At half-past ten, while the Republican Guards played a triumphal march, the President entered with Mme Pasteur on his arm. The whole assembly rose. Great applause greeted simultaneously the head of the State, and the man of science who, by his long sustained exertions, had brought wealth and glory to France."

Many speeches were made, many addresses presented. The president of the Academy of Science was able to say to Pasteur that every word of praise in every tongue had been used in his honour; the Permanent Secretary, Joseph Bertrand, made the following remark: ". . . If, in this company assembled in honour of your scientific achievements, one were to ask: What is M. Pasteur's greatest discovery? the cleverest would be at a loss for a reply. Each of your great works shines with such brilliance that, on studying it and regarding it closely, one is tempted to think that it eclipses all the others; all are illuminated by the same light, the same accurate, extensive and sound science is their basis and support."

Lister had come to represent the Royal Society of London and the Royal Society of Edinburgh. When the great English surgeon rose, the students greeted him with a *ban*, the rhythmic applause which is their highest expression of admiration and enthusiasm. Lister said to Pasteur:

"I have the great honour of presenting to you the homage of Medicine and Surgery.

"Truly there does not exist in the whole world an individual to whom Medical Science owes more than to you.

"Your researches on fermentations threw a powerful light which has illuminated the dark places in surgery and has changed the treatment of wounds from an uncertain, empiric and too often disastrous business into a scientific and certainly beneficial art. Thanks to you, surgery has undergone a complete revolution which has deprived it of all its terrors, and which has increased its efficacy to an almost unlimited extent.

"Medicine owes not less than surgery to your profound and philosophic studies. You have raised the veil which for centuries had covered infectious diseases;

you have discovered and demonstrated their microbic nature. Thanks to your initiative, and in many cases to your own personal work, we already thoroughly understand the causes of a large number of these pernicious disorders :

"*Felix qui potest rerum cognoscere causas !*

"This knowledge has already perfected to a surprising extent the diagnosis of these scourges of the human race, and has pointed out the road which must be followed in their prophylactic and curative treatment.

"On this road your splendid discoveries on the attenuation and reinforcement of virus, serve and will always continue to serve, as guiding stars.

"As a brilliant example I may quote your studies on rabies. Their originality was so striking, in pathology as in therapy, that many doctors at first regarded you with suspicion. Is it possible, they said, that a man who is neither a doctor nor a biologist can give us information with regard to a disease on which the most distinguished lights in medicine have exercised their brains in vain ?

"*Quis novus hic nostris successit sedibus hospes ?*

"With regard to myself, I recognized too well the brilliance of your genius, the scrupulous carefulness of your instructions, and your absolute honesty, to be able to share such unworthy sentiments for a moment. My confidence has been justified by the event. With the insignificant exception of a few ignoramuses, the whole world now recognizes the grandeur of your achievements in combating this terrible malady. You have furnished a diagnosis which banishes in a moment the agony of uncertainty which formerly tortured one who had been bitten by a healthy dog suspected of rabies. This alone would have sufficed to draw upon you the everlasting gratitude of humanity ; but, by your marvellous system of anti-rabies inoculations, you have known how to pursue and conquer the poison after its entrance into the body.

"Monsieur Pasteur, infectious diseases constitute, as you know, the greater number of the maladies to which the human race is subject. You can therefore, well understand why it is, that on this impressive occasion, medicine and surgery hasten to bring you the profound homage of their admiration and gratitude."

This speech provoked an indescribable manifestation of enthusiasm. Pasteur rose to embrace Lister. The sight of these two men, clasped in each others arms, says an eye-witness, seemed a living symbol of the fraternity of science in the alleviation of the sufferings of humanity.

The mayor of Dôle presented to Pasteur two photographs, one reproducing his birth-certificate, whereon was to be seen the signature of his father, the other, the house where he was born; he recalled Pasteur's devotion to his home, and the touching words in which he had handed on to his parents the homage rendered to himself. "During the whole of this speech Pasteur remained with his face hidden in his hands. Those who knew him intimately were aware of the devotion with which he honoured his father and mother. Their memory thus abruptly invoked moved him to tears. His emotion was so deep that the whole hall shared it."

Pasteur was too much moved, and his voice too weak, for him to make himself heard unaided. His son read his speech of thanks:

"Monsieur le President of the Republic,

"Your presence works a transformation: a small celebration becomes a great festival, and the simple birthday of a man of science will remain, thanks to you, a date to be observed in the history of the science of France.

"Gentlemen, you have had the ingenious and tactful idea of trying to make my whole life pass before my eyes. One of my compatriots of the Jura, the mayor of Dôle, had brought me the photograph of the humble house where my father and mother led such a laborious existence. The presence of all the pupils of the École Normale reminds me of dazzling moments of my earliest scientific enthusiasms. The representatives of the Faculty of Lille recall those first studies in crystallography and fermentations which opened a whole new world to me . . . .

"You, finally, the delegates of foreign nations, who have come so far to prove your sympathy with France, you bring me the greatest joy which a man can feel, who firmly believes that science and peace must triumph over ignorance and war, that nations will unite not to destroy but to instruct one another, and that the future will belong to those who have done most for suffering humanity. I refer to you, my dear Lister, and to all you representatives of science, medicine and surgery. . . .

"Gentlemen, I express to you my profound emotion and my deepest gratitude. As Roty, the great artist, has on the reverse of this medal decked with roses the number of the years that weigh so heavily upon me, so you, my dear colleagues, have rejoiced my old age with the sight of all this vigorous and affectionate youth. . . ."

The anonymous publisher of *The Jubilee of M. Pasteur* has concluded with a few lines which, by a piece of good luck rare in official documents, tell the simple and whole truth: "Such was the morning of December 27, 1892. All those present experienced a joy deeper and more generous than they had ever felt in all their lives. The soul of France was to be found in the assembly, inspired with the most noble and disinterested feelings—admiration and gratitude. It was a unique spectacle in which a great man was, in Shakespeare's beautiful phrase, 'carried in triumph on the hearts of all.'"

bies

As Vulpian and Lister said, Pasteur had had, with regard to rabies, no precursor. His principal conquests in this unexplored domain may be summarized in a few lines:

The virus exists not only in the saliva of the mad dog, but also and more particularly in the nervous matter of the brain and of the spinal cord.

Intercranial inoculation of the virus of ordinary rabies produces the disease after a period of about a fortnight.

The virus is reinforced by passage through rabbits, and a maximum virulence is thus attained which permits rabies to be developed after seven days incubation.

This virus can be attenuated to any degree by the action of oxygen.

In inoculating a series of attenuated viruses from nil to the maximum, rabies can be prevented the more certainly the sooner the inoculations take place after the bite.

These discoveries followed and were connected with one another with perfect regularity, and it seems as if they must have been made quite naturally in this order. Nevertheless they took five years of stubborn work. Many times it happened that an experiment gave a quite disconcerting result: Let us do it again, Pasteur would say, it is essential not to drop the subject.

This exertion wore him out. His collaborator Roux wrote: "he bore the period of determined research, better than the excitement of victory. . . . As soon as the preventive inoculations were applied to man, he lost all power of repose. Each bitten patient absorbed him afresh. The sight of injured children caused him an emotion which he could never get over. When hopeless cases, for whom no treatment was of any use, arrived, Pateur felt all their sufferings. Each visit he paid them was a torture to him, yet he could not prevent himself from visiting them."

Soon Pasteur had to give up work in the laboratory. This was a great grief to him.

He had, however, the great pleasure of seeing Roux, the Sub-Director of his Institute, originate in France the serotherapy of diphtheria, which was to save so many children who would formerly have died of this hideous disease.

His pupil Yersin went to China to look for the microbe of plague, and one could already foresee the discovery of anti-plague serum.

Thus in spite of his own failing powers, Pasteur saw his work growing and spreading.

He passed a last summer at Villeneuve-l'Étang, on the estate where he had installed his kennels for the study of rabies, and where stables were being built for horses intended to provide the anti-diphtheric serum.

Soon the end came. René Vallery-Radot has given a touching account of Pasteur's last days.

" . . . All through his life he had practised the Gospel virtues. He reverenced the faith of his fathers, and wished, without ostentation or mystery, to receive its aid during this last period."

" . . . His weakness was extreme. On September 27th, when someone leant over his bed to offer him a cup of milk: 'I cannot,' he said disconsolately. His look had an indescribable expression of resignation, of benevolence, of farewell. His head sank back on the pillow; he fell asleep. After this deceptive repose, suddenly the short laboured breathing of the last agony began. For twenty-four hours he lay motionless, his body almost entirely paralysed, his eyes closed. One of his hands lay in that of Mme Pasteur or some other relation, the other held a crucifix. In this room, which had something of the simplicity of a monk's cell, on Saturday, September 28, 1895, surrounded by his family and his disciples, at four o'clock in the afternoon, very gently he expired."

CHAPTER XXXVIII

PASTEUR'S WORK

ABOVE all things Pasteur loved light. Obscurity in a scientific question seemed to him like a disorder; he felt an imperative desire to understand and to see clearly.

Even as a boy at college, he had agitated by his questions a poor old professor whose only way of teaching was to make his class learn the text book by heart, and who thought an enquiring pupil a very disagreeable creature.

At the École Normale, Pasteur was haunted by a note of Mitscherlich, which declared that two bodies absolutely identical in appearance had nevertheless inverse action on polarized light. He remained persuaded that this appearance was illusory, and he sought the reason of this illusion, until he discovered in the crystals, which were supposed to be identical in form, that difference which neither Mitscherlich nor Biot had been able to see. This was the starting-point of his numerous studies on molecular dyssymmetries, the importance and productiveness of which was to be demonstrated in the near future.

The course of Pasteur's career as professor led him to Lille, where the manufacture of alcohol from beetroot was one of the chief industries of the locality. This alcohol is produced by a fermentation which all the scientists, and particularly Liebig and Berzelius, the chief chemists of the day, considered to be a purely chemical action. Pasteur's work on crystallography and his studies in rotatory power did not agree with this statement: he did not hesitate to think that Liebig and Berzelius were wrong, and it was in endeavouring to prove their error that he discovered the laws of fermentation and recognized the real nature of ferments.

The study of ferments led him to the discovery of anaerobes; he was then able to give a complete explanation of the dissolution of organic matter. It is life which presides over the work of death, and the dissolution of animal or vegetable matter, "this unceasing return to the atmosphere and to the mineral kingdom of the elements which animals and vegetables have borrowed from them, are actions correlative to the development and multiplication of organic beings."

Whence do ferments come? Pasteur asked himself this question and thus met with the epidemics which were ruining sericulturists; and not only did he find the means to avoid these epidemics and to restore to sericulture its ancient prosperity, but he also drew from his observations information which was most useful in human pathology.

He was not slow in the application of these new ideas, and discoveries went on multiplying.

Pasteur studied successively, or simultaneously, anthrax, the vibrion-septique, the microbes of osteomyelitis and puerperal infection, chicken-cholera, and the microbe of this last disease, which seemed of so little interest, led him to one of his most marvellous discoveries: vaccination, which inaugurated a new era in medicine.

Thanks to vaccination he conquered anthrax, *rouget*, and rabies. The victory over rabies, that most dreaded of diseases, lifted Pasteur into indisputable fame. He had risen by progressive steps by studies which were all, in spite of their diversity, connected and supported by one another.

One may seek in vain for a work which can be compared with his and for discoveries from which we have reaped greater benefits.

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